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**EPIX**  
PHARMACEUTICALS

## ANNUAL REPORT 2007

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## EPIX PHARMACEUTICALS, INC. Michael G. Kauffman, Chief Executive Officer

The past year has been an exciting one for EPIX. We made significant progress, achieving many corporate goals and advancing our clinical programs. The strong foundation built in 2007 has positioned the company for continued growth in 2008.

As we look back at 2007, we are proud of the exciting positive data we announced and the milestones we achieved under our strategic partnerships:

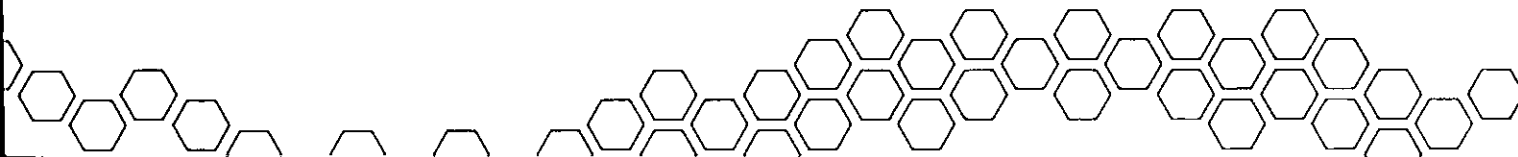
- **Positive Phase 2a Data in Alzheimer's Disease for PRX-03140** – our CNS active 5-HT<sub>4</sub> agonist increases acetylcholine in the brain and in this trial showed statistically-significant improvements in the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) after only two weeks
- **Positive Phase 2a Data for PRX-08066, a first-in-class 5-HT<sub>2B</sub> antagonist in PH associated with COPD** – our first-in-class 5-HT<sub>2B</sub> antagonist demonstrated statistically significant reductions in systolic pulmonary artery pressure (SPAP) in patients with Pulmonary Hypertension (PH) associated with Chronic Obstructive Pulmonary Disease (COPD)
- **Positive Phase 1b Data for PRX-07034 in Obesity and Cognitive Impairment** – our novel 5-HT<sub>6</sub> antagonist met the primary safety and tolerability endpoints with statistically significant results in obesity and cognitive function
- **Milestone Achievements with GlaxoSmithKline (GSK)** – we reached initial milestones in the first and second of three discovery stage programs with GSK
- **Milestone Achievements with Cystic Fibrosis Foundation Therapeutics (CFFT)** – we reached the third and fourth milestones of our recently-expanded collaboration with CFFT

Our goal at EPIX is to continue to build upon our corporate and clinical success and to further leverage the efficiency and productivity of our *in silico* drug development platform. We have already begun to do this in the first quarter and will continue our efforts throughout the year.

We recently announced the findings of our Phase 2b clinical trial of PRX-00023 in major depressive disorder (MDD). We were disappointed that this trial, while continuing to demonstrate PRX-00023's very favorable safety profile, did not achieve statistically significant efficacy. As a result, we have discontinued our development of PRX-00023 so that we may focus our drug development efforts and resources on our other promising product candidates.

The early part of this year has brought us increased regulatory clarity on Vasovist®. We have initiated the re-read of images obtained in previously conducted Phase 3 trials. This is as a result of our agreement with the U.S. Food and Drug Administration (FDA) on our proposal for this re-read of images of our novel blood pool magnetic resonance angiographic agent, Vasovist. We're very pleased with the progress we've made with the FDA, and we expect to resubmit our New Drug Application to the FDA in the middle of 2008. Vasovist has already been approved for marketing in 33 countries outside of the United States, based on approvals by five independent regulatory bodies. We look forward to working with the FDA and our strategic partner for this program, Bayer Schering Pharma, to make Vasovist available to patients in the United States.

Additionally, we are making great progress in our promising Alzheimer's disease program as we continue to collaborate with our strategic partner GlaxoSmithKline. Building on the results seen in our Phase 2a clinical trial, we have announced that we will initiate two Phase 2b clinical trials of PRX-03140 in Alzheimer's disease with GSK in the first half of this year. These two studies will consist of a monotherapy trial and a trial studying PRX-03140 in combination with donepezil, and both studies will address a larger patient population and a longer duration of therapy than our previous two-week Phase 2a trial. There are currently more than five million people in United States living with Alzheimer's disease, and the cost of this debilitating condition is estimated at \$148 billion annually. Because Alzheimer's patients progress from mild to severe memory loss and



can suffer from an inability to communicate and care for themselves, the emotional toll of this disease on patients and their families and caregivers is also significant. We are excited about the potential shown by our PRX-03140 program in an area of such dire need for safe and effective treatments.

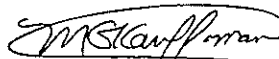
By mid-2008, we also expect to initiate a Phase 2b right-heart catheter study of PRX-08066 in secondary pulmonary hypertension. We believe that this is a promising area of medicine with increasing patient populations but no currently approved drugs. Our PRX-08066 is a first-in-class compound and we believe that it has tremendous potential to address one of the world's fastest growing diseases. COPD is estimated to become the third leading cause of mortality worldwide within the next 10 years and PH is estimated to be present in approximately 20% of COPD patients. Most experts believe that about half of these patients with COPD and secondary PH, or about 1 million people in the United States, would benefit from treatment of their PH.

Finally, this year we plan to initiate a study in cognitive impairment for our 5-HT6 antagonist, PRX-07034, with the Treatment Units for Research on Neurocognition and Schizophrenia (TURNS) group in the third quarter of this year. We are moving the development of this program forward in cognitive impairment based upon its statistically significant Phase 1b results and safety profile. Late last year, EPIX was selected by TURNS, part of the U.S. National Institute of Mental Health, for a future clinical trial to be conducted in conjunction with TURNS. TURNS assesses and selects those compounds it feels are important to the study and treatment of neurocognitive disorders and schizophrenia.

We are proud to be working with TURNS to develop a trial protocol and timeline, with a collaborative Phase 2a study expected to start later this year. Additionally, we remain interested in obesity based on our statistically significant data previously reported, and will be working on backup compounds to PRX-07034 for use in other indications.

We believe our 2007 accomplishments have enabled us to establish a solid clinical and collaborative foundation as EPIX continues to grow and evolve. We have built this foundation while facing clinical development challenges and weathering volatile capital markets. Despite these challenges we have continually worked to realize the value of EPIX for our shareholders. We believe that this year will be key as EPIX continues its efforts to achieve and communicate a steady stream of data and corporate milestones. We look forward to sharing our future achievements with you.

We thank you for your continued support.



**Michael G. Kauffman, MD, PhD**  
Chief Executive Officer

#### Forward Looking Statements

The information contained herein includes forward-looking statements intended to qualify for the safe harbor from liability established by the Private Securities Litigation Reform Act of 1995. These statements relate to, among other things, our expectations concerning our research and development efforts, regulatory compliance, commercial strategy, strategic alliances and collaborative efforts, sales and reimbursement efforts and their likely future success. Some of the forward-looking statements can be identified by the use of forward-looking terms such as "believes," "expects," "may," "will," "should," "seek," "intends," "plans," "estimates," "anticipates," or other comparable terms. Forward-looking statements involve inherent risks and uncertainties. A number of important factors could cause actual results to differ materially from those in the forward-looking statements. We urge you to consider the risks and uncertainties discussed in greater detail under the heading "Risk Factors" in this Annual Report in evaluating our forward-looking statements. We have no plans to update our forward-looking statements to reflect events or circumstances after the date of this report. We caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made.

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

- ☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d)  
OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2007

OR

- ☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d)  
OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

SEC  
Mail Processing  
Section

APR 7 2008

Commission file number: 0-21863

**EPIX PHARMACEUTICALS, INC.** <sup>100</sup>

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of  
incorporation or organization)

04-3030815

(I.R.S. Employer  
Identification No.)

4 Maguire Road, Lexington, Massachusetts

(Address of principal executive offices)

02421

(Zip Code)

Registrant's telephone number, including area code:

(781) 761-7600

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of Each Class

Name of Each Exchange on Which Registered

Common Stock, \$0.01 par value per share

The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Exchange Act:

NONE

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☐ Accelerated filer ☒ Non-accelerated filer ☐ Smaller reporting company ☐  
(Do not check if a smaller reporting company)

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold as of the last business day of the registrant's most recently completed second fiscal quarter was \$127,091,000.

As of March 14, 2008, the registrant had 41,355,575 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the Registrant's Proxy Statement for the 2008 Annual Meeting of Stockholders.

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Our name and corporate logo are trademarks of EPIX Pharmaceuticals, Inc. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

## PART I

*This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, and are subject to the "safe harbor" created by those sections. These statements relate to, among other things, our expectations concerning our research and development efforts, regulatory compliance, commercial strategy, strategic alliances and collaborative efforts, sales and reimbursement efforts and their likely future success. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. Some of the forward-looking statements can be identified by the use of forward-looking terms such as "believes," "expects," "may," "will," "should," "seek," "intends," "plans," "estimates," "anticipates," or other comparable terms. Accordingly, these statements involve estimates, assumptions and uncertainties that could cause actual results to differ materially from those expressed in them. Our actual results may differ significantly from the results discussed in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those set forth in "Item 1A. Risk Factors" and elsewhere in this Annual Report on Form 10-K. We have no plans to update our forward-looking statements to reflect events or circumstances after the date of this report. We caution readers not to place undue reliance upon any such forward-looking statements, which speak only as of the date made.*

### ITEM 1. BUSINESS

#### OVERVIEW

We are a biopharmaceutical company focused on discovering, developing and commercializing novel pharmaceutical products through the use of proprietary technology to better diagnose, treat and manage patients. We have four internally discovered therapeutic product candidates in clinical trials. These drug candidates are targeting conditions such as depression, Alzheimer's disease, cardiovascular disease and cognitive impairment. Our blood-pool imaging agent, Vasovist, is approved for marketing in more than 30 countries outside of the United States. We also have collaborations with SmithKline Beecham Corporation (GlaxoSmithKline), Amgen Inc., Cystic Fibrosis Foundation Therapeutics, Incorporated, and Bayer Schering Pharma AG, Germany. Our business strategy is to develop our internally discovered, novel pharmaceutical products through the point of proof of clinical concept, typically completion of Phase 2 clinical trials and then to seek pharmaceutical partnerships for the continued development, regulatory approvals and world-wide commercialization of the product candidates. In certain disease areas, such as pulmonary hypertension, where we believe we can efficiently obtain regulatory approval and effectively market the product through a specialty sales force, we may seek to retain commercialization rights in the United States.

The focus of our therapeutic drug discovery and development efforts is on the two classes of drug targets known as G-protein Coupled Receptors, or GPCRs, and ion channels. GPCRs and ion channels are classes of proteins embedded in the surface membrane of all cells and are responsible for mediating much of the biological signaling at the cellular level. We believe that our proprietary drug discovery technology and approach addresses many of the inefficiencies associated with traditional GPCR and ion channel-targeted drug discovery. By integrating computer-based, or in silico, technology with in-house medicinal chemistry, we believe that we can rapidly identify and optimize highly selective drug candidates. We focus on GPCR and ion channel drug targets whose role in disease has already been demonstrated in clinical trials or in preclinical studies. In each of our four clinical-stage therapeutic programs, we used our drug discovery technology and approach to optimize a lead compound into a clinical drug candidate in less than ten months, synthesizing fewer than 80 compounds per program. We moved each of these drug candidates into clinical trials in less than 18 months from lead identification. We believe our drug discovery technology and approach enables us to efficiently and cost-effectively discover and develop GPCR and ion channel-targeted drugs.

We expanded into the development of therapeutic drug products through our acquisition of Predix Pharmaceuticals Holdings, Inc., or Predix, in August 2006. Predix was incorporated in Delaware on November 2, 1994. Throughout this Annual Report on Form 10-K, except where otherwise stated or indicated by the context, "we," "us," or "our" means EPIX Pharmaceuticals, Inc. and its consolidated subsidiaries and their predecessors (including Predix).

## OUR PRODUCT CANDIDATES

The following chart summarizes the status of our clinical drug development programs as of March 14, 2008:

Product	Target	Lead Discovery	Lead Optimization	IND/ GLP Tox	Phase I	Phase 2	Phase 3	NDA	Approved
<b>PRX-00023</b>	<b>(5-HT1A)</b>	Depression							
<b>PRX-03140</b>	<b>(5-HT4)</b>	Alzheimer's Disease (GSK has exclusive option)							
<b>PRX-08066</b>	<b>(5-HT2B)</b>	Pulmonary Hypertension in COPD							
<b>PRX-07034</b>	<b>(5-HT6)</b>	Cognitive Impairment							
<b>Vasovist*</b>	<b>Vessels</b>	Vascular Imaging (Bayer Schering Pharma AG, Germany)							

\* Vasovist is approved for marketing in more than 30 countries outside of the United States. For a description of the collaboration agreement with Bayer Schering Pharma AG, Germany, see "Business — Strategic Alliances and Collaborations" below.

## THERAPEUTICS

Through the application of our GPCR and ion channel drug discovery expertise, over the past five years we have created a pipeline of drug candidates designed to address diseases with significant unmet medical needs and commercial potential across a range of therapeutic areas.

### PRX-00023 for Depression

We are currently developing PRX-00023, a novel, highly selective, small-molecule 5-HT1A agonist for the treatment of depression. In March 2007, we initiated a Phase 2b clinical trial to evaluate the efficacy of PRX-00023 in patients with a primary diagnosis of Major Depressive Disorder (MDD) who also have concurrent anxiety. The randomized, double-blind, placebo-controlled trial completed enrollment in October 2007, enrolling 362 adult patients with MDD, and is designed to evaluate the effect of treatment with up to 120 mg of PRX-00023 twice-daily for eight weeks as determined by the change from baseline in the Montgomery Asberg Depression Rating Scale (MADRS) compared with placebo. All patients randomized to the drug treatment began with 40 mg PRX-00023 twice daily, and would increase the dose, if tolerated, to a maximum of 120 mg twice daily within the first week. Changes in the Hamilton Anxiety Score (HAM-A), Clinical Global Impressions Improvement Scale (CGI-I) and Clinical Global Severity of Illness Scale (CGI-S) were also measured. Results of the study are expected to be reported in March 2008. To date, there have been no serious adverse events associated with treatment in more than 300 subjects who have received PRX-00023.

During the fourth quarter of 2006, we completed a dose escalating study of PRX-00023 in healthy volunteers where we explored doses up to 320 mg, either as a single daily dose or as 160 mg given twice per day for three weeks. PRX-00023 was well tolerated with no serious adverse events or discontinuations. This study indicated that PRX-00023 at doses up to 320 mg per day may be well tolerated.

In September 2006, we completed a 310 patient, Phase 3 double-blind, placebo controlled, multi-center clinical trial for the treatment of generalized anxiety disorder with PRX-00023. Results from this trial demonstrated that PRX-00023 did not achieve a statistically significant improvement over placebo for the primary endpoint of efficacy with respect to generalized anxiety disorder at the dose tested (80 mg once daily). The mean HAM-A score change from baseline to week eight with PRX-00023 treatment was 9.8, compared to

a mean HAM-A change of 8.5 from baseline to week eight with placebo ( $p=0.116$ ). A p-value represents the probability that a difference observed between groups during an experiment happened by chance. For example, a p-value of  $p=0.05$  means there is a 5% probability that the result occurred by chance. In general, clinical scientists regard p-values of less than 0.05 to be "statistically significant," and p-values greater than 0.05 to be insignificant. Effects of PRX-00023 on symptoms of depression, which was a secondary endpoint of the Phase 3 clinical trial, were assessed using the MADRS, an FDA-recommended assessment for depression. The data from this trial showed a statistically significant ( $p=0.009$ ) improvement from baseline with PRX-00023 treatment compared to placebo in the MADRS score, indicating that PRX-00023 reduced symptoms of depression present in the patients in this trial. In this Phase 3 trial, PRX-00023 was well tolerated, and the rate of discontinuation due to adverse events was very low (1.4% with PRX-00023 vs. 2.9% with placebo). Based on the Phase 3 trial results, we have discontinued clinical development of PRX-00023 at a dose of 80 mg once daily in generalized anxiety disorder. We are currently focusing our development efforts for this drug candidate on depression.

#### *PRX-03140 for Alzheimer's disease*

PRX-03140 is a novel, highly selective, small-molecule 5-HT<sub>4</sub> agonist that we are developing for the treatment of Alzheimer's disease. PRX-03140 is being developed to provide improved cognition and to potentially slow Alzheimer's disease progression. We completed a Phase 2 trial of PRX-03140 alone and in combination with an approved drug for Alzheimer's disease (the cholinesterase inhibitor Aricept (donepezil)) in patients with Alzheimer's disease in the fourth quarter of 2007. This randomized, double-blind, placebo-controlled, multiple ascending dose trial enrolled 80 patients with mild Alzheimer's disease. Patients were studied on PRX-03140 across three dose groups of 10 patients each: 50 mg once-daily, 150 mg once-daily and placebo, or in a placebo-controlled combination across five dose arms of 10 patients each: PRX-03140 at 5, 25, 50, 100 and 200 mg with Aricept 10 mg once-daily.

The two primary endpoints of the trial were: (1) to assess the safety and tolerability of PRX-03140 in patients with Alzheimer's disease when dosed orally once-daily for 14 days alone and in combination with donepezil, and (2) to assess the effect of PRX-03140 on brain wave activity, as was performed in the Phase 1b clinical trial. Secondary endpoints of the trial included evaluating the pharmacokinetic effect of PRX-03140 on Aricept concentrations in patients with mild Alzheimer's disease and assessing the effects of repeat doses of PRX-03140 on a battery of standardized cognitive function tests, such as the Alzheimer's Disease Assessment Scale cognitive subscale (ADAS-cog). ADAS-cog is the current standard for evaluating drug efficacy for cognition in Alzheimer's disease and is an established and accepted FDA registration endpoint.

Efficacy results show that patients receiving 150 mg of PRX-03140 orally once daily as monotherapy achieved a mean 3.6 point improvement on the ADAS-cog versus a 0.9 point worsening in patients on placebo. This result corresponds to a p-value of 0.021, which is statistically significant. Data for the patients on a 50 mg dose of PRX-03140 showed a 1.0 point improvement on the ADAS-cog. The monotherapy dose response (150 mg versus 50 mg versus placebo) was also statistically significant ( $p=0.026$ ). ADAS-cog changes in the combination arms of the trial were not statistically significant.

This trial also used Mindstreams, an automated battery of computerized cognitive function tests, as a secondary endpoint. Patients on PRX-03140 monotherapy demonstrated statistically significant ( $p<0.04$ ) improvements in memory and visual-spatial indices as measured using Mindstreams when compared with placebo. PRX-03140 also produced positive trends in the alteration in brain wave activity in the 150 mg dose group versus placebo, similar to the changes observed with currently approved drugs for Alzheimer's disease.

Based upon the improvements in cognition demonstrated over 14 days of dosing, we received requests from certain patients, caregivers and clinical trial investigators for continued access to PRX-03140. We have accommodated such requests on a case-by-case basis by extending the study to allow these patients to continue on PRX-03140.

PRX-03140 appeared to be well tolerated in this trial, both alone and in combination with Aricept. No serious drug-related adverse events occurred during the trial.

Pursuant to a development and license agreement entered into on December 11, 2006, we granted GlaxoSmithKline an option to obtain exclusive, worldwide license rights to complete the development of, and commercialize, PRX-03140. For a description of the collaboration agreement with GlaxoSmithKline, see "Business — Strategic Alliances And Collaborations" below.

#### *PRX-08066 for Pulmonary Hypertension*

PRX-08066 is a novel, highly selective, small-molecule inhibitor, or antagonist, of a specific GPCR known as 5-HT<sub>2B</sub>. We are developing PRX-08066 for the treatment of two types of pulmonary hypertension: pulmonary arterial hypertension; and pulmonary hypertension associated with chronic obstructive pulmonary disease. Pulmonary hypertension, or PH, in general is a serious, often fatal cardiovascular disease characterized by elevation of pulmonary blood pressure and progressive thickening and narrowing of the blood vessels of the lungs, often leading to heart failure. We completed a Phase 2 trial of PRX-08066 in pulmonary hypertension associated with chronic obstructive pulmonary disease, or COPD, in August 2007. This randomized, double-blind, placebo-controlled Phase 2 trial enrolled 71 patients with PH associated with COPD. Patients were randomized to one of three arms; 200 mg of PRX-08066 once-daily; 400 mg of PRX-08066 once-daily; or placebo. The two-week double-blind phase of the study was followed by an open label extension in which 10 patients received 200 mg daily for six weeks. The primary endpoints of the trial were safety and tolerability of PRX-08066.

Efficacy was measured by the effect of PRX-08066 compared to placebo on systolic pulmonary artery pressure, or SPAP, and included 62 evaluable patients who completed the double-blind portion of the study. In a population where decreases of 3 mmHg to 4 mmHg in a post-exercise SPAP are considered clinically significant, the results showed a statistically significant dose-response for the patients that demonstrated a decrease of 4 mmHg or more. In the 400 mg dose group, 45% of the patients had a reduction in post-exercise SPAP of 4 mmHg or more versus 14% on placebo ( $p=0.043$ ). An analysis of SPAP changes in all subjects revealed a dose trend with median reductions of 1.2 mmHg and 3.38 mmHg in the 200 mg and 400 mg dose groups, respectively, compared with no change on placebo. PRX-08066 was generally well-tolerated. There were no serious adverse events considered related to PRX-08066, and the majority of adverse events were mild or moderate in nature. One subject in the 200 mg dose group who then continued into the six-week open-label extension experienced a modest increase in liver enzyme levels at the end of the extension that was believed to be drug-related. These values returned to normal within two weeks and the subject remained asymptomatic.

We have completed three Phase 1 clinical trials of PRX-08066 in healthy volunteers, including a Phase 1b clinical trial in athletes conditioned to exercise at high altitudes. Results from the Phase 1b trial showed that, compared with placebo, PRX-08066 caused a statistically significant reduction in the increase in systolic pulmonary blood pressure observed during exercise in volunteers breathing low oxygen. In the two earlier Phase 1 trials as well as the Phase 1b trial, PRX-08066 was well-tolerated, with a half-life of approximately 16 hours, supporting once daily oral dosing. To date, there have been no serious adverse events associated with treatment with PRX-08066.

#### *PRX-07034 for Cognitive Impairment associated with Schizophrenia and Alzheimer's disease*

PRX-07034 is a novel, highly selective, small-molecule antagonist of a specific GPCR known as 5-HT<sub>6</sub>. PRX-07034 is being developed for the treatment of cognitive impairment associated with schizophrenia and Alzheimer's disease. We are also working on back-up compounds for use in other indications such as obesity.

In April 2007, we completed a Phase 1 multiple ascending dose clinical trial studying the safety, tolerability, pharmacokinetics, and pharmacodynamics of PRX-07034 administered once-daily for 28 days in a population of 33 otherwise healthy obese adults with body mass indices, or BMI, between 30 and 42 kg/m<sup>2</sup>. Normal BMI is less than 25 kg/m<sup>2</sup>. PRX-07034 demonstrated predictable pharmacokinetics with dose proportional increases in exposures, and a half-life supporting once-daily dosing. Signals suggestive of pharmacologic activity were observed for obesity with a greater proportion of subjects on drug experiencing weight loss during the one month period than subjects on placebo. Overall results on cognitive function as

measured by the CogScreen test battery, showed a dose dependent trend for improvement. For the predetermined cognitive endpoint that combines speed and accuracy, there was a statistically significant improvement at the 600 mg dose once daily. Subsequently, an independent external analysis of the CogScreen test battery results confirmed a significant drug effect on cognition but was not able to confirm the dose-dependent trend. No dose limiting toxicity was identified, and no serious adverse events were reported.

In October 2007, we completed a randomized, double-blind, placebo-controlled Phase 1 trial of 21 obese, but otherwise healthy, adults. Findings from this study demonstrated that adults taking 600 mg of PRX-07034 twice-daily for 28 days had a weight reduction of an average of 0.45 kg (approximately 1 pound), while adults on placebo gained 1.37 kg (approximately 3 pounds) during the same period, which was statistically significant ( $p < 0.005$ ). Subjects in the study were not required to follow any pre-specified diet or exercise program. PRX-07034 was associated with a statistically significant ( $p = 0.036$ ) reduction in serum leptin levels, a marker of fat stores in the body. Overall, only one of the subjects (approximately 10%) on placebo lost any weight during the trial, while 7 of the 11 subjects (approximately 64%) on PRX-07034 lost weight. PRX-07034 appeared well-tolerated and there were no serious adverse events reported. An increase in corrected QT interval, or QTc, was apparent at the dose tested, however, with a mean increase over the duration of the study of 10.7 milliseconds for the drug group versus a decrease of 1.7 milliseconds for the placebo group. The corrected QTc is a measurement of the QT interval, which is corrected for heart rate. Prolongations of the QTc are associated with an increased risk for potentially life-threatening heart rhythms and so this measurement is an important index to measure during the development of new drugs. In addition, of the population of 21 adults, one patient on drug discontinued due to a rash that resolved rapidly. There were no discontinuations on placebo. In the prior Phase 1 trial where doses up to 600 mg once daily were studied for 28 days, no clinically meaningful prolongations of the QTc were noted.

The 21-person trial, which was conducted in an outpatient setting (subjects spent three nights of the total 28-day trial as inpatients to accommodate measurements and physical examinations), included secondary endpoint measures to assess potential effects on body weight, hunger, satiety and exploratory endpoint measures of cognitive function. An analysis of cognitive data in this study showed no difference between drug and placebo at a dose of 600 mg twice daily. Accordingly, future studies in cognitive impairment are expected to utilize doses less than 600 mg twice daily based on the study results and the positive data in cognition previously demonstrated in lower doses.

Safety and tolerability data from an earlier single ascending dose Phase 1 trial completed in healthy adult male and female volunteers indicated that single doses of PRX-07034 were well tolerated up to 2500 mg, the highest dose tested. In addition, PRX-07034 demonstrated adequate absorption, with drug exposures increasing with increasing doses and a half-life of 14 to 24 hours. Preclinical animal models of obesity suggested that this drug candidate may reduce both food intake and body weight. In addition, preclinical animal models of memory impairment suggest that PRX-07034 may have cognitive-enhancing properties.

## **IMAGING AGENT**

### *Vasovist*

Vasovist is an internally discovered, injectable intravascular contrast agent that is designed to provide improved imaging of the vascular system using magnetic resonance angiography or MRA. Our target indication for Vasovist is for use in MRA imaging of peripheral vascular disease, with a goal of improving the physician's ability to visualize the human vascular system and thereby enhance disease diagnosis and treatment. As of December 31, 2007, Vasovist has been approved for marketing in more than 30 countries outside of the United States.

Vasovist reversibly binds to the human blood protein albumin, allowing imaging of the blood vessels for approximately an hour after administration. With a single injection, Vasovist enables the capture of three-dimensional images of arteries and veins in the body. Vasovist may make it possible for physicians to detect vascular disease earlier, more safely and less invasively than with X-ray angiography, and for physicians to provide an improved evaluation of potential therapeutic options including percutaneous intervention and vascular surgery.

In December 2003, we submitted a New Drug Application, or NDA, to the FDA for the use of Vasovist in detection of vascular disease. In January 2005 and November 2005, we received approvable letters from the FDA for Vasovist pending additional clinical trials. After considering the parameters of the additional clinical trials requested by the FDA, we filed a formal appeal with the FDA requesting approval of Vasovist, as well as the use of an advisory committee as part of the appeal process, which was denied in August 2006. We met with the FDA after receiving the August 2006 response letter and in February 2007 we filed a second formal appeal with the FDA requesting approval of Vasovist, as well as the use of an advisory committee as part of the appeal process. In June 2007, we received a response letter from the FDA on our second formal appeal. While denying the immediate approval of Vasovist, the FDA indicated that a blinded re-read of the images obtained from the previously completed Phase 3 clinical trials of Vasovist could support approval of Vasovist if the results are positive. In January 2008, we initiated the re-read of the images obtained in prior Phase 3 studies conducted for Vasovist. We expect to complete the re-read of the prior Phase 3 studies in the first half of 2008 and plan to submit the results to the FDA in mid 2008.

## OUR THERAPEUTIC DRUG DISCOVERY TECHNOLOGY AND APPROACH

We have developed a novel and proprietary *in silico* protein structure-based approach to GPCR and ion channel-targeted drug discovery that allows us to benefit from the structure-based approach in the absence of experimentally-determined structures for these targets. Our PREDICT technology combines genomic information (the amino acid sequence of the target protein) with physical and chemical properties of the cell membrane environment to determine the most stable 3D structure of a membrane-bound protein. The use of our PREDICT technology to determine a 3D structure of the target protein is the foundation and first step in our novel system of discovery and optimization for GPCR and ion channel-targeted drugs. We maintain our GPCR and ion channel structures as trade secrets, which, when combined with our proprietary software and the know-how required to use the PREDICT technology, we believe creates a strong barrier to entry for our competitors.

Using our proprietary drug discovery technology and approach requires the successive application of the following five steps: (1) using our PREDICT technology to identify the most stable 3D structure of the desired GPCR or ion channel drug target, bypassing the need for X-ray crystallography, (2) analyzing the resulting 3D structure and identifying a potential binding site on the target structure for drug interaction, (3) performing *in silico* screening using the computer to virtually "fit" more than two million drug-like compounds into this drug site, ensuring that both the shape and chemical properties of the binding site and the compound match, (4) selecting the approximately 100-200 compounds that best match the binding site on the target and testing their activity *in vitro* in the laboratory and (5) identifying the most active and novel chemical compounds, referred to as lead compounds, and then subjecting these lead compounds to an integrated structure-based lead optimization process. The PREDICT-generated 3D structure of the target protein as well as other 3D protein structures (many of which are also generated by PREDICT) and more traditional medicinal chemistry efforts are used to steer lead optimization along the most efficient path, transforming lead compounds into drug candidates expeditiously. Our discovery and optimization process is outlined in the following steps:

- *PREDICT-3D in silico modeling.* We have developed novel proprietary algorithms which we use in our PREDICT technology to model the 3D structure of targets of interest (GPCRs and ion channel proteins) from their primary amino acid sequence. PREDICT uses algorithms that explore a large number of possible structures of the target and then selects the biologically relevant one. It takes into account specific interactions between the target protein and the membrane, specific interactions within the target protein itself, and addresses the limitations that hamper homology-based modeling of GPCRs and ion channel proteins. The PREDICT software code and many of its algorithms are kept as trade secrets, making it difficult to copy or reverse engineer. We filed patent applications for PREDICT version 1.0 in 2000. The current version of PREDICT has evolved considerably from the original version and includes numerous new algorithms and capabilities. PREDICT bypasses the need for X-ray crystallography structures of the GPCR or ion channel protein target to initiate a structure-based (so-called "rational") drug discovery program.

- *Virtual libraries.* Our libraries consist of in silico versions of four million drug-like compounds which are available for purchase from commercial vendors worldwide. These virtual libraries reduce the need for us to synthesize or purchase, store and maintain tens or hundreds of thousands of actual compounds for the initial screening.
- *Rapid in silico screening.* The process of in silico screening requires the computer to perform trillions of operations in trying to fit numerous drug-like compounds into the binding site of the target protein, matching both shape and chemical properties. We perform high-throughput in silico screening with a combination of proprietary and commercially available public software to identify compounds that may bind to a target GPCR or ion channel protein.
- *Ranking of screening results.* We have developed proprietary algorithms for ranking our in silico screening results using internally developed tools, which we believe enables us to select the 100-200 most promising compounds for in vitro testing.
- *Integrated structure-based lead optimization.* The most promising novel lead compounds, identified in silico and shown to have binding affinity and functionality in vitro, are optimized into drug candidates using an integrated structure-based approach. This process makes use of the PREDICT 3D structures (of the drug target and related off-target proteins) as well as many other in silico tools that we have created or acquired to enable efficient structure-based lead optimization, leading to highly selective drug candidates. These tools allow us to overcome challenges frequently encountered during lead optimization, such as selectivity, blood-brain barrier penetration and hERG ion channel binding, in a fraction of the time and cost compared to traditional lead optimization efforts. Using these in silico tools, our computational and medicinal chemists are able to select for actual synthesis the most promising subset of suggested compounds for further optimization. In each of our clinical-stage programs, this approach has allowed us to synthesize fewer than 10% of the compounds that we believe would have been synthesized if we were to follow the traditional methods of lead optimization.

## STRATEGIC ALLIANCES AND COLLABORATIONS

### *GlaxoSmithKline*

On December 11, 2006, we entered into a development and license agreement with SmithKline Beecham Corporation, doing business as GlaxoSmithKline, and Glaxo Group Limited to develop and commercialize medicines targeting four G-protein coupled receptors, or GPCRs, for the treatment of a variety of diseases, including an option to license our 5-HT<sub>4</sub> partial agonist, PRX-03140. The other three GPCR targets identified under the collaboration are new discovery programs. GlaxoSmithKline does not have options to any of our other clinical programs besides PRX-03140. Our collaboration with GlaxoSmithKline is being conducted through its Center of Excellence for External Drug Discovery.

Pursuant to the collaboration agreement, we granted GlaxoSmithKline an exclusive option to obtain exclusive, worldwide license rights to complete the development and to commercialize the products initially developed under each of our four research programs under the collaboration agreement. In return for those options and in consideration of the development work to be performed by us under the collaboration agreement, GlaxoSmithKline paid us an initial payment of \$17.5 million. Additionally, as part of the collaboration, on December 11, 2006, we entered into a stock purchase agreement with GlaxoSmithKline providing for the issuance and sale to GlaxoSmithKline of 3,009,027 shares of our common stock for an aggregate purchase price of \$17.5 million. In addition, we may be eligible for up to an aggregate of \$1.2 billion in additional nonrefundable option fees and milestone payments relating to the achievement of certain development, regulatory and commercial milestones across the four research programs. To date, we have received an aggregate of \$6 million in such milestone payments related to identifying a total of six lead candidates, three from each of the first two discovery programs, to move forward into lead optimization. We are also eligible to receive tiered, double-digit royalties based on net sales by GlaxoSmithKline of any products developed under the collaboration agreement. The specific royalty rates will vary depending upon a number of factors, including the total annual net sales of the product and whether it is covered by one of our patents. GlaxoSmithKline's royalty obligation under the collaboration agreement generally terminates on a

product-by-product and country-by-country basis upon the later of (i) the expiration of our last patent claiming the manufacture, use, sale or importation of the product in the relevant country and (ii) twelve years after the first commercial sale of the product in the relevant country. GlaxoSmithKline accounted for 53% of our revenue in the year ended December 31, 2007.

If GlaxoSmithKline does not exercise any of the four options, the collaboration agreement will expire upon the expiration of the last such option. Otherwise, the collaboration agreement will expire on a product-by-product and country-by-country basis upon the expiration of the royalty payment obligations for each product in each country.

Under the collaboration agreement, we have agreed to design, discover and develop, at our own cost, small molecule drug candidates targeting four GPCRs. The design, discovery and development efforts will be guided by a joint steering committee formed pursuant to the collaboration agreement. The first program is focused on the 5-HT4 receptor and will include our 5-HT4 partial agonist drug candidate, PRX-03140, which is currently in Phase 2 clinical development for the treatment of Alzheimer's disease. We have retained an option to co-promote products successfully developed from the 5-HT4 program in the United States. Under any such co-promotion arrangement, the collaboration agreement provides for GlaxoSmithKline to direct the promotional strategy and compensate us for our efforts in co-promoting the product. We have ongoing research activities for each of the three additional GPCR targets identified under the collaboration.

We have responsibility and control for filing, prosecution or maintenance of any of our patents that are the subject of an option to GlaxoSmithKline under the collaboration agreement, provided that in the event an option is exercised, responsibility and control of the patents subject to such option transfers to GlaxoSmithKline.

The parties each have the right to terminate the collaboration agreement if the other party becomes insolvent or commits an uncured material breach of the collaboration agreement. In addition, GlaxoSmithKline has the right to terminate the collaboration agreement in its entirety, and to terminate its rights to any program developed under the collaboration agreement on a regional or worldwide basis, in each case without cause. Upon a termination of the collaboration agreement, depending upon the circumstances, the parties have varying rights and obligations with respect to the grant of continuing license rights, continued commercialization rights and continuing royalty obligations.

### ***Amgen***

On July 31, 2006, we entered into an exclusive license agreement with Amgen Inc. to develop and commercialize products based on our preclinical compounds that modulate the S1P1 receptor and compounds and products that may be identified by or acquired by Amgen and that modulate the S1P1 receptor. The S1P1 receptor is a cell surface GPCR found on white blood cells and in other tissues that is associated with certain autoimmune diseases, such as rheumatoid arthritis and multiple sclerosis.

Pursuant to the license agreement, we granted Amgen an exclusive worldwide license to our intellectual property and know-how related to the compounds in our S1P1 program that modulate the S1P1 receptor, for the development and commercialization of those compounds and other compounds and products that modulate the S1P1 receptor. Amgen has limited rights to sublicense its rights under the license. In return for the license, Amgen paid us a nonrefundable, up-front payment of \$20 million and is obligated to pay us royalties based on aggregate annual net sales of all S1P1-receptor-modulating products developed by Amgen under the license agreement. In addition, we may be eligible for up to an aggregate of \$287.5 million of nonrefundable milestone payments that relate to milestones associated with the commencement of clinical trials, regulatory approvals and annual net sales thresholds of the products under the license agreement. These royalty rates and milestone amounts are subject to reduction in the event that, among other things:

- Amgen is required to obtain third-party rights to develop and commercialize a product that incorporates an EPIX compound; and

- Amgen develops and commercializes products that are not covered by the intellectual property rights we licensed to Amgen, such as for example, S1P1-modulating products that may be acquired by Amgen from a third-party.

Generally, Amgen's royalty obligation under the agreement terminates on a product-by-product and country-by-country basis upon the later of (a) the expiration or termination of the last claim within the patents (whether such patents are patents EPIX licensed to Amgen or are patents owned or in-licensed by Amgen) covering such product and (b) ten years following the first commercial sale of the product. The agreement expires when all of Amgen's royalty obligations have terminated.

We have the option to co-promote one product from the collaboration in the United States for one indication to be jointly selected by EPIX and Amgen. During the first 15 months of the agreement, we were required to design, discover and develop, at our own cost, additional compounds that modulate the S1P1 receptor and that are within the same family of compounds as those identified in our patent applications licensed to Amgen under the agreement. The collaboration agreement provides Amgen with a license to these additional compounds to further its development efforts. We may undertake additional research under the agreement, at our own expense, as approved by a joint steering committee formed pursuant to the agreement. We have responsibility and control for filing, prosecution or maintenance for any of our patents licensed to Amgen for 24 months or until the start of Phase 1 clinical trials for the first product developed under the agreement, at which time, responsibility and control of such patents transfers to Amgen. Amgen has responsibility and control for filing, prosecution or maintenance for all other patents covered by the agreement, including patents jointly developed under the agreement. Amgen will have final decision making authority on all other research matters and will be responsible for non-clinical and clinical development, manufacturing, regulatory activities and commercialization of the compounds and products developed under the license agreement, at its own expense.

The parties each have the right to terminate the agreement (in whole or for specified products or countries, depending upon the circumstances) upon a material uncured breach by the other party and Amgen has the right to terminate the agreement for convenience upon varying periods of at least three months advance notice. Upon a termination of the agreement, depending upon the circumstances, the parties have varying rights and obligations with respect to the grant of continuing license rights, continued commercialization rights and continuing royalty obligations.

#### ***Bayer Schering Pharma AG, Germany***

In June 2000, we entered into a strategic collaboration agreement with Bayer Schering Pharma AG, Germany pursuant to which we granted Bayer Schering Pharma AG, Germany an exclusive license to co-develop and market Vasovist worldwide, excluding Japan. In December 2000, we amended this strategic collaboration agreement to grant to Bayer Schering Pharma AG, Germany the exclusive rights to develop and market Vasovist in Japan. Generally, each party to the agreement will share equally in Vasovist costs and profits in the United States. Under the agreement, we retained responsibility for completing clinical trials and filing for FDA approval in the United States and Bayer Schering Pharma AG, Germany is responsible for clinical and regulatory activities for the product outside the United States. In addition, we granted Bayer Schering Pharma AG, Germany an exclusive option to develop and market an unspecified vascular MRI blood pool agent from our product pipeline. In connection with this strategic collaboration and the amendment to our strategic collaboration agreement with Covidien (formerly Tyco International Ltd.), as described under "Intellectual Property" below, Bayer Schering Pharma AG, Germany paid us an up-front fee of \$10 million, which we then paid to Covidien. Under the agreement, Bayer Schering Pharma AG, Germany also paid us \$20 million in exchange for shares of our common stock. We may be eligible for up to an additional \$23.2 million upon the achievement of certain milestones, including \$1.3 million that may be earned if Vasovist is approved in the United States. We also are entitled to receive a royalty on products sold outside the United States and, if Vasovist is approved and launched in the United States, a percentage of Bayer Schering Pharma AG, Germany's operating profit margin on products sold in the United States.

Under the terms of the strategic collaboration agreement with Bayer Schering Pharma AG, Germany, either party may terminate the agreement upon thirty days notice if there is a material breach of the contract. In addition, Bayer Schering Pharma AG, Germany may terminate the agreement at any time on a region-by-region basis or in its entirety, upon six months written notice to us.

In May 2003, we entered into a broad alliance with Bayer Schering Pharma AG, Germany for the discovery, development and commercialization of molecularly-targeted contrast agents for MRI. The alliance was composed of two areas of collaboration, with one agreement generally providing for exclusive development and commercialization collaboration for EP-2104R, our product candidate for the detection of thrombus, and the second agreement covering an exclusive research collaboration to discover novel compounds for diagnosing human disease using MRI. Under the first agreement, Bayer Schering Pharma AG, Germany had an option to the late stage development and worldwide marketing rights for EP-2104R. On July 12, 2006, Bayer Schering Pharma AG, Germany notified us that it declined to exercise this option. As a result, we retained commercial rights to EP-2104R. In the event EP-2104R is commercialized, we are obligated to pay Bayer Schering Pharma AG, Germany a royalty which is limited to a portion of the funding we received for this program from Bayer Schering Pharma AG, Germany. The second agreement related to a broader research collaboration under which the research jointly pursued under the agreement concluded in May 2006.

On May 8, 2000, we granted to Bayer Schering Pharma AG, Germany a worldwide, royalty-bearing license to patents covering Bayer Schering Pharma AG, Germany's development project, Primovist, an MRI contrast agent for imaging the liver, which was approved in the European Union in 2004. Under this agreement, Bayer Schering Pharma AG, Germany is required to pay us royalties based on sales of products covered by this agreement. This agreement expires upon the last-to-expire patent covered by the agreement unless terminated earlier by either party because of the material breach of the agreement by the other party. Also on May 8, 2000, Bayer Schering Pharma AG, Germany granted us a non-exclusive, royalty-bearing license to certain of its Japanese patents. Under this agreement, we are required to pay Bayer Schering Pharma AG, Germany royalties based on sales of products covered by this agreement. This agreement expires upon the last-to-expire patent covered by the agreement unless terminated earlier by either party because of the material breach of the agreement by the other party.

#### *Cystic Fibrosis Foundation Therapeutics, Incorporated*

In March 2005, we entered into a research, development and commercialization agreement with Cystic Fibrosis Foundation Therapeutics, Incorporated, or CFFT, the drug discovery and development affiliate of the Cystic Fibrosis Foundation. In August 2006, we expanded the research, development and commercialization agreement with CFFT. In November 2007, the agreement was further amended to provide for approximately \$1.1 million of research funding for the Cystic Fibrosis Transmembrane conductance Regulator, or CFTR, program until the parties negotiate a follow-on agreement for the further discovery and development of the CFTR program. As of December 31, 2007, we have received an aggregate of \$11.9 million in payments under the agreement. The agreement originally consisted of two development programs as follows:

- The first program is focused on correcting a malfunction of the CFTR ion channel protein. We are using our proprietary structure-based technologies to model the structure of this ion channel protein target and identify binding sites in the channel for therapeutic intervention. Once these sites are identified, we aim to use our drug discovery capabilities to discover a drug that restores proper functionality to the channel in patients with cystic fibrosis. Based upon the results of the program, we have agreed with the CFFT to negotiate towards a follow-on agreement under which we will explore a structure-based approach for the discovery and commercialization of a drug that will target CFTR, with the financial support of CFFT and subject to a royalty payable to CFFT.
- The second program is focused on the discovery of a small-molecule agonist to the G-Protein Coupled Receptor known as P2Y(2), which plays a role in cystic fibrosis, using our proprietary structure-based drug design system. We retain the right to develop and commercialize any drug candidates discovered through this second program, and are obligated to make aggregate royalty payments of up to

\$15.0 million to CFFT for the first drug candidate that reaches particular regulatory and sales milestones.

The agreement expires with respect to the first program on August 2, 2009. The second program expired during 2007. CFFT may terminate the CFTR program without cause upon 120 days notice or if we suspend or discontinue our business. Either party may terminate the agreement for an uncured material breach. CFFT accounted for 25% of our revenue in the year ended December 31, 2007.

## TECHNOLOGY AGREEMENTS

### *Covidien (formerly Tyco International Ltd.)*

In August 1996, we entered into a strategic collaboration agreement with Mallinckrodt Inc. (subsequently acquired by Covidien Ltd.), involving research, development and marketing of MRI vascular contrast agents developed or in-licensed by either party. In June 2000, in connection with the exclusive license that we granted to Bayer Schering Pharma AG, Germany under our strategic collaboration agreement, we amended our strategic collaboration with Covidien. The amendment enabled us to sublicense certain technology from Covidien to Bayer Schering Pharma AG, Germany which allowed us to enter into the strategic collaboration agreement for Vasovist with Bayer Schering Pharma AG, Germany. Pursuant to that amendment, we also granted to Covidien a non-exclusive, worldwide license to manufacture Vasovist for clinical development and commercial use on behalf of Bayer Schering Pharma AG, Germany in accordance with a manufacturing agreement entered into in June 2000 between Covidien and Bayer Schering Pharma AG, Germany. In connection with this amendment, we paid Covidien an up-front fee of \$10.0 million and are obligated to pay up to an additional \$5.0 million in milestone payments, of which \$2.5 million was paid following the NDA filing in February 2004 and \$2.5 million is required to be paid upon any U.S. product approval. We are also required to pay Covidien a share of our Vasovist operating profit margins in the United States and a percentage of the royalty that we receive from Bayer Schering Pharma AG, Germany on Vasovist gross profits outside the United States.

### *Bracco*

In September 2001, pursuant to a settlement and release agreement and worldwide license agreement, we granted Bracco a worldwide, non-exclusive royalty bearing sub-license to certain of our patents. Under the terms of the license fee, we received \$10.0 million in 2001 and are entitled to receive royalty payments from Bracco on their sales of MultiHance. The royalty on sales of MultiHance expired on the patent expiration date in each country in which MultiHance is sold. We received our final royalty payment from Bracco in the second quarter of 2007.

## COMPETITION

We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies engaged in drug discovery activities or funding, both in the United States and abroad. Some of these competitors are pursuing the development of product candidates that target the same indications that we are targeting for our clinical and preclinical programs. Even if we and our collaborators are successful in developing our clinical-stage candidates, the resulting products will compete with a variety of established products.

Significant competitors in the area of GPCR-focused drug discovery include Arena Pharmaceuticals, Acadia Pharmaceuticals, Addex Pharmaceuticals and 7TM Pharma, and for ion channels our competitors include Vertex Pharmaceuticals and Sucampo Pharmaceuticals. In addition, most large pharmaceutical companies have drug discovery programs that target GPCRs and ion channels.

Many of our competitors have significantly greater financial, manufacturing, marketing and product development experience and resources than we do. These companies also have significantly greater research and development capabilities than we do, and have significantly greater experience than we do in preclinical and clinical trials of potential pharmaceutical products, and in obtaining FDA and other regulatory clearances.

Our commercial opportunity will be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer side effects or are less expensive than any products that we may develop.

If our clinical-stage drug candidates are approved, they will compete with currently approved drugs and potentially with drug candidates currently in development for the same indications, including the following:

- *PRX-00023*. If approved, PRX-00023, the drug candidate we are developing for the treatment of depression, may compete with approved products from such pharmaceutical companies as Forest Laboratories, Inc., GlaxoSmithKline plc, Eli Lilly & Co., Pfizer Inc. and Wyeth, and may compete with drug candidates in clinical development from other companies, including Sanofi-Aventis.
- *PRX-03140*. If approved, PRX-03140, the drug candidate we are developing for the treatment of Alzheimer's disease, may compete with approved products from such pharmaceutical companies as Forest Laboratories, Inc., Johnson & Johnson, Novartis AG and Pfizer, Inc., and may compete with drug candidates in clinical development from other companies, including Myriad Genetics, Inc., GlaxoSmithKline plc and Neurochem Inc. We are studying PRX-03140 both as monotherapy and in combination with approved products, such as Aricept which is marketed by Pfizer Inc.
- *PRX-08066*. If approved, PRX-08066, the drug candidate we are developing for the treatment of pulmonary arterial hypertension (PAH), may compete with approved products from such pharmaceutical companies as Actelion Pharmaceuticals Ltd., GlaxoSmithKline plc, Pfizer Inc., Gilead Sciences Inc., and United Therapeutics Corporation, and may compete with drug candidates in clinical development by other companies, such as Encysive Pharmaceuticals Inc. and Bayer Schering Pharma AG.
- *PRX-07034*. If approved for the treatment of cognitive impairment (associated with schizophrenia or Alzheimer's disease), PRX-07034 may compete with approved products from such pharmaceutical companies as Forest Laboratories, Johnson & Johnson, Novartis AG and Pfizer, Inc., and may compete with several therapeutic product candidates in clinical development from other companies, including GlaxoSmithKline plc, AstraZeneca and Memory Pharmaceuticals Corp. If approved for the treatment of obesity, PRX-07034 may compete with approved products from such pharmaceutical companies as Abbott Laboratories and Roche Holding Ltd., and may compete with several therapeutic product candidates in clinical development by other companies, such as Sanofi-Aventis and Arena Pharmaceuticals, Inc.
- *Vasovist*. There are a number of general use MRI agents approved for marketing in the United States and in certain foreign markets that, if used or developed for MR angiography, are likely to compete with Vasovist. Such products include Magnevist and Gadovist by Bayer Schering Pharma AG, Germany, Dotarem by Guerbet, S.A., Omniscan by GE Healthcare, ProHance and MultiHance by Bracco and OptiMARK by Covidien Ltd. We are aware of certain agents under clinical development that have been or are being evaluated for use in MRA: Bayer Schering Pharma AG, Germany's Gadomer and SHU555C, Guerbet, S.A.'s Vistarem, Bracco's B-22956/I, Ferropharm GmbH's Code VSOP-C184, and Advanced Magnetix, Inc.'s Ferumoxytol. In addition to competition within the MRI field, we also face competition from other imaging technologies, including CT scans, ultrasounds, and X-ray scans.

## INTELLECTUAL PROPERTY

We actively seek to protect the proprietary technology that we consider important to our business, including chemical species, compositions and formulations, their methods of use and processes for their manufacture, as new intellectual property is developed. In addition to seeking patent protection in the United States, we plan to selectively file patent applications in certain additional foreign countries in order to further protect the inventions that we consider important to the development of our foreign business. We also rely upon trade secrets and contracts to protect our proprietary information.

As of February 28, 2008, our patent portfolio included a total of 16 issued U.S. patents, 117 issued foreign patents and 277 pending patent applications in the United States and other countries with claims covering the composition of matter and methods of use for all of our clinical-stage candidates and Vasovist. In addition to patents, we rely where necessary upon unpatented trade secrets and know-how and continuing

technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, employees and consultants and invention assignment agreements with our employees. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

In addition, we license, and expect to continue to license, third-party technologies and other intellectual property rights that are incorporated into some elements of our drug discovery and development efforts. Set forth below are our significant license agreements.

### ***Ramot***

Our proprietary drug discovery technology and approach is in part embodied in technology that we license from Ramot at Tel Aviv University Ltd., the technology transfer company of Tel Aviv University. Pursuant to this license, we have exclusive, worldwide rights to certain technology developed at Tel Aviv University to develop, commercialize and sell products for the treatment of diseases or conditions in humans and animals. The licensed technology, as continually modified, added to and enhanced by us, consists in large part of computer-based models of biological receptors and methods of designing drugs to bind to those receptors.

All of our current clinical-stage therapeutic drug candidates, PRX-00023, PRX-03140, PRX-08066 and PRX-07034, were, at least in part, identified, characterized or developed using the licensed technology, and we would be required to make payments to Ramot, as described below, if and when rights to any such drug candidates are ever sublicensed or any such drug candidates are commercialized. In addition, we have used the licensed technology in all of our preclinical-stage programs and would expect to make payments to Ramot if rights to any drug candidates were ever commercialized from any of these programs. One of our employees, Sharon Shacham, Senior Vice President of Drug Development, was one of the inventors of the technology that we license from Ramot. We believe that Ramot shares a portion of any royalty income received with the respective inventors and, accordingly, Dr. Shacham receives a portion of the amounts we pay Ramot.

We paid Ramot an upfront fee of \$40,000 upon the grant of the license. Under the license, we have an obligation to make royalty payments to Ramot on our net sales of products that are identified, characterized or developed through the use of the licensed technology that are either 1.5% or 2.5% of such net sales (depending upon the degree to which the product needed to be modified after being identified, characterized or developed through the use of the licensed technology) and decrease as the volume of sales increases. The royalty obligation for each product expires on a country-by-country basis twelve years after the first commercial sale. There is also an annual minimum royalty payment obligation of \$10,000 per year.

We also are required to share between 5% and 10% of the consideration we receive from parties to whom we grant sublicenses of rights in the Ramot technology or sublicenses of rights in products identified, characterized or developed with the use of such technology and between 2% and 4% of consideration we receive from performing services using such technology. In connection with our collaborations with GlaxoSmithKline, Amgen and Cystic Fibrosis Foundation Therapeutics, Incorporated, we have to date paid \$2.6 million in total royalties to Ramot primarily for the total payments received to date for the upfront payments and milestone payments received under these license agreements.

The license may be terminated by either party upon a material breach by the other party unless cured within 30 days, in the case of a payment breach, and 90 days in the case of any other breach. The license may also be terminated by either party in connection with the bankruptcy or insolvency of the other party. The license expires upon the expiration of our obligation to make payments to Ramot. Therefore, since we have an ongoing obligation to pay annual minimum royalties to Ramot as described above, the license may not expire and may only terminate upon a breach by, or bankruptcy of, a party.

### ***Massachusetts General Hospital***

In July 1995, we entered into a license agreement with Massachusetts General Hospital, or MGH pursuant to which MGH granted us an exclusive worldwide license to patents and patent applications which relate to Vasovist. The MGH license imposed certain due diligence obligations with respect to the development of products covered by the license, all of which have been fulfilled to date. The MGH license requires us to pay royalties on the net sales of products covered by this license, including Primovist, MultiHance and Vasovist. We have paid MGH approximately \$0.6 million in royalty payments, primarily related to the sale of Primovist and MultiHance, through 2007 under this license agreement. The license agreement expires on a country-by-country basis when the patents covered by the license agreement expire, the majority of which expired in November 2006. The license agreement does not contain a renewal provision. We believe that the expiration of these patents does not compromise our proprietary position with respect to Vasovist because Vasovist is covered by composition of matter patents independent of our license with MGH. These composition of matter patents extend into 2015 in the United States, although the life of these patents may be extended.

### ***Prince***

In November 2003, we entered into an intellectual property agreement with Martin R. Prince, M.D., Ph.D., an early innovator in the field of magnetic resonance angiography relating to "dynamic" magnetic resonance angiography, which involves capturing magnetic resonance angiography images during the limited time, typically 30 to 60 seconds, available for imaging with extracellular agents. Under the terms of the intellectual property agreement, Dr. Prince granted us certain discharges, licenses and releases in connection with the historic and future use of Vasovist by us and agreed not to sue us for intellectual property infringement related to the use of Vasovist. In consideration of Dr. Prince entering into the agreement, we agreed to pay him an upfront fee of \$850,000 and royalties on sales of Vasovist consistent with a non-exclusive early stage academic license and delivered to him 88,000 shares of our common stock with a value of approximately \$2.3 million based on the closing price of our common stock on the date of the agreement. In addition, we agreed to supply Dr. Prince with approximately \$140,000 worth of Vasovist per year during the term of the agreement. The agreement expires upon the expiration of the last patent under the agreement. The agreement is subject to termination by either party upon the incurred material breach of the agreement by the other party. As of December 31, 2007, no Vasovist product has been requested by or provided to Dr. Prince.

## **MARKETING, SALES AND DISTRIBUTION**

We currently have no marketing, sales or distribution capabilities. To commercialize any of our drug candidates or imaging products, we must develop these capabilities internally or through collaboration with third-parties. In selected indications where we believe that our products can be commercialized by a specialty sales force that calls on a limited but focused group of physicians, we may commercialize our products in the United States. For example, we believe that pulmonary specialists who treat pulmonary hypertension, and the centers in which they practice, are sufficiently concentrated to enable us to effectively promote PRX-08066, if approved by the FDA, to this market in the United States with a small internal sales force. In therapeutic or diagnostic areas that require a large sales force selling to a large and diverse prescribing population and for markets outside of the United States, we plan to establish collaborations with pharmaceutical or biotechnology companies for commercialization of our drug candidates. With respect to Vasovist, we have granted Bayer Schering Pharma AG, Germany an exclusive license to co-develop and market Vasovist worldwide under our strategic collaboration agreement with Bayer Schering Pharma AG, Germany. With respect to PRX-03140, we have granted GlaxoSmithKline an exclusive option to obtain exclusive, worldwide license rights to complete the development and commercialization of PRX-03140. With respect to our preclinical compounds that modulate the SIP1 receptor, we have granted Amgen an exclusive worldwide license for the development and commercialization of those compounds.

## MANUFACTURING

We outsource and plan to continue to outsource manufacturing responsibilities to third-parties for our existing and future drug candidates for clinical development and commercial purposes. We are currently working with our contract manufacturers to produce sufficient quantities of the active pharmaceutical ingredient and drug product in each of our programs for our planned clinical trials in 2008. If one of our manufacturers for our therapeutic product candidates should become unavailable to us for any reason, we believe that there are a number of potential replacements as our processes are not manufacturer-specific, though we may incur some added cost and delay in identifying or qualifying such replacements, including delays associated with the need for FDA review and approval of the new manufacturer, as well as those associated with the new manufacturer's ability to establish the manufacturing process.

Bayer Schering Pharma AG, Germany is responsible for the manufacture of Vasovist. Bayer Schering Pharma AG, Germany relies on Covidien as the sole manufacturer of Vasovist for human clinical trials and commercial use. Together with Bayer Schering Pharma AG, Germany, EPIX is considering alternative manufacturing arrangements for Vasovist for commercial use, including the potential transfer of manufacturing to Bayer Schering Pharma AG, Germany. In the event that Covidien fails to fulfill its manufacturing responsibilities satisfactorily, Bayer Schering Pharma AG, Germany has the right to purchase Vasovist from a third-party or to manufacture the compound itself.

We currently rely on Aptuit, Inc. and Thermo Fisher Scientific Inc. for our therapeutic drug product manufacturing and testing, and on Aptuit, Inc. (formerly Evotec, Ltd.) and Johnson Matthey Pharma Services for the manufacture and testing of our active therapeutic pharmaceutical ingredients. Our agreements with these suppliers generally operate on a work order basis, with no minimum purchase requirements and are generally terminable by us upon 60 days and 90 days prior written notice, respectively. Small amounts of material used for preclinical research and development purposes are synthesized in-house or with third-party contract laboratories. The production of our drug candidates PRX-08066, PRX-00023, PRX-03140 and PRX-07034 uses small-molecule synthetic organic chemistry procedures that are standard in the pharmaceutical industry. There are no complicated chemistries or unusual equipment required in the manufacturing process of these drug candidates. PRX-08066, PRX-00023, PRX-03140 and PRX-07034 are all currently administered as unformulated drug products. A commercially viable formulation will need to be developed, manufactured and certified for each of these drug candidates. The final commercial formulation may not prove to be bioequivalent to the current formulation. This may result in the need to initiate additional clinical trials to define new dosing regimes. Furthermore, the development and implementation of a new formulation and commercial process for cGMP manufacturing may add significant delays to additional clinical trials, regulatory filings and commercial launch.

## GOVERNMENT REGULATION AND PRODUCT APPROVAL

The FDA and comparable regulatory agencies in state and local jurisdictions and in foreign countries impose substantial requirements upon the clinical development, manufacture and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate, among other things, the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, advertising and promotion of our products. Failure to comply with regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other actions that could affect our product candidates or us. Any failure to comply with regulatory requirements, to obtain and maintain regulatory approvals, or any delay in obtaining regulatory approvals could materially adversely affect our business.

The process required by the FDA before drugs may be marketed in the United States generally involves the following:

- preclinical laboratory and animal studies;
- submission of an investigational new drug application, or IND, which must become effective before human clinical trials may begin;

- adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use; and
- FDA approval of a new drug application, or NDA.

The testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for any of our drug candidates will be granted on a timely basis, if at all.

Once a pharmaceutical candidate is identified for development it enters the preclinical testing stage. During preclinical studies, laboratory and animal studies are conducted to show biological activity of the drug candidate in animals, both healthy and with the targeted disease. Also, preclinical tests evaluate the safety of drug candidates. Preclinical tests must be conducted in compliance with good laboratory practice regulations. In some cases, long-term preclinical studies are conducted while clinical studies are ongoing.

Prior to commencing a clinical trial, we must submit an IND to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions about the conduct of the trial. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Our submission of an IND may not result in FDA authorization to commence a clinical trial. All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with good clinical practice regulations. These regulations include the requirement that all subjects provide informed consent. Further, an institutional review board, or IRB, at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if adverse events or other certain types of changes occur.

Human clinical trials are typically conducted in three sequential phases that may overlap:

- *Phase 1:* The drug is initially introduced into healthy human subjects or patients with the disease and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion.
- *Phase 2:* Involves studies in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- *Phase 3:* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide, if appropriate, an adequate basis for product labeling.

In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients. Because these patients already have the target disease, these studies may provide initial evidence of efficacy traditionally obtained in Phase 2 clinical trials, and thus these trials are frequently referred to as Phase 1/2 clinical trials.

The FDA or an IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Concurrent with clinical trials and preclinical studies, companies also must develop information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and the manufacturer must develop methods for testing the quality, purity and potency of the final drugs. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf-life.

A sponsor of an IND may request that the FDA evaluate within 45 days certain protocols and issues relating to the protocols. Such Special Protocol Assessments, or SPAs, may be requested for clinical protocols

for Phase 3 clinical trials whose data will form the primary basis for an efficacy claim if the trials had been the subject of discussion at an end-of-Phase 2 / pre-Phase 3 meeting. If the sponsor and the FDA reach a written agreement regarding the protocol, the SPA will be considered binding on the FDA and will not be changed unless the sponsor fails to follow the agreed-upon protocol, data supporting the request are found to be false or incomplete, or the FDA determines that a substantial scientific issue essential to determining the safety or effectiveness of the drug was identified after the testing began. Even if a SPA is agreed to, approval of the NDA is not guaranteed since a final determination that an agreed-upon protocol satisfies a specific objective, such as the demonstration of efficacy, or supports an approval decision, will be based on a complete review of all the data in the NDA.

The results of product development, preclinical studies and clinical studies, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, results of chemical studies and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The FDA reviews all NDAs submitted before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under certain circumstances. The FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

The FDA has various programs, including fast track, priority review and accelerated approval that are intended to expedite or simplify the process for reviewing drugs and/or provide for approval on the basis of surrogate endpoints. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, priority review applies to new drugs that have the potential for providing significant improvements compared to marketed products in the treatment or prevention of a disease. Although priority review does not affect the standards for approval, FDA will attempt to expedite review of the application for a drug designated for priority review. We do not know whether our drugs will be eligible for, or whether we will apply for, any of these programs. Even if a drug qualifies for one or more of these programs, we cannot be sure that the time period for FDA review will be shortened.

Satisfaction of FDA requirements or similar requirements of state, local and foreign regulatory agencies typically takes at least several years and the actual time required may vary substantially, based upon, among other things, the type, complexity and novelty of the product or disease. Government regulation may delay or prevent marketing of potential products for a considerable period of time and impose costly procedures upon our activities. Success in early-stage clinical trials does not assure success in later-stage clinical trials. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. Even if a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delays in obtaining, or failures to obtain regulatory approvals for any drug candidate could substantially harm our business and cause our stock price to drop significantly. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, drug sampling and distribution requirements, notifying the FDA and gaining its approval of certain manufacturing or labeling changes, complying with certain electronic records and signature

requirements and complying with FDA promotion and advertising requirements. Drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon us and our contract manufacturers. We cannot be certain that we or our present or future suppliers will be able to comply with the pharmaceutical cGMP regulations and other FDA regulatory requirements.

The FDA's policies may change and additional government regulations may be enacted which could prevent or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of adverse governmental regulation, which might arise from future legislative or administrative action, either in the U.S. or abroad.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process. If a product that has orphan drug designation subsequently receives FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, also could block the approval of our product for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our product is determined to be contained within the competitor's product for the same indication or disease. We intend to file for orphan drug designation for those diseases that meet the criteria for orphan designation, including for PRX-08066 for the treatment of pulmonary hypertension. There is no guarantee that we will be awarded orphan exclusivity for PRX-08066 or for any other products or indications. In addition, obtaining FDA approval to market a product with orphan drug exclusivity may not provide us with a material commercial advantage.

The FDA Modernization Act of 1997 included a pediatric exclusivity provision that was extended by the Best Pharmaceuticals for Children Act of 2002. Pediatric exclusivity is designed to provide an incentive to manufacturers for conducting research about the safety of their products in children.

Pediatric exclusivity, if granted, provides an additional six months of market exclusivity in the U.S. for new or currently marketed drugs. Under Section 505a of the Federal Food, Drug and Cosmetic Act, six months of market exclusivity may be granted in exchange for the voluntary completion of pediatric studies in accordance with an FDA-issued "Written Request." The FDA may issue a Written Request for studies on unapproved or approved indications, where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may produce health benefits in that population. We have not requested or received a Written Request for such pediatric studies, although we may ask the FDA to issue a Written Request for such studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies and submit reports of the studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles. There is no guarantee that the FDA will issue a Written Request for such studies or accept the reports of the studies.

## **REIMBURSEMENT**

Sales of our product candidates depend in significant part on the availability of third-party reimbursement. We anticipate third-party payors will provide reimbursement for our therapeutic and imaging products. It is time consuming and expensive for us to seek reimbursement from third-party payors. Reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

The passage of the Medicare Prescription Drug and Modernization Act of 2003, or the MMA, imposes new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries, which may affect the marketing of our products. The MMA also introduced a new reimbursement methodology, part of

which went into effect in 2004. At this point, it is not clear what effect the MMA will have on the prices paid for currently approved drugs and the pricing options for new drugs approved after January 1, 2006. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

In addition, in some foreign countries, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market.

We expect that there will continue to be a number of federal and state proposals to implement governmental pricing controls. While we cannot predict whether such legislative or regulatory proposals will be adopted, the adoption of such proposals could have a material adverse effect on our business, financial condition and profitability.

## **EMPLOYEES**

We believe that our success will depend greatly on our ability to identify, attract and retain capable employees. As of December 31, 2007, we had 119 full-time employees, including a total of 60 employees who hold M.D. or Ph.D. degrees. Of our employees, 93 are primarily engaged in research and development activities, and 26 are primarily engaged in general and administrative activities. Our employees are not represented by any collective bargaining unit, and we believe our relations with our employees are good.

## **RESEARCH AND DEVELOPMENT**

During the years ended December 31, 2007, 2006, and 2005 we incurred research and development expenses of \$57.5 million, \$149.8 million and \$18.3 million, respectively. Included in our 2006 research and development expense is a nonrecurring charge of \$123.5 million for the acquisition of in-process research and development in connection with our acquisition of Predix Pharmaceuticals Holdings, Inc. The in-process research and development charge represents the fair value of purchased in-process technology of Predix for research projects that, as of the closing date of the merger, had not reached technological feasibility and have no alternative future use.

## **AVAILABLE INFORMATION**

We incorporated in Delaware in 1988 as Metacorp, Inc. and commenced operations in 1992. After changing our name to Metasyn Inc. in 1989 and EPIX Medical, Inc. in 1996, we changed our name to EPIX Pharmaceuticals, Inc. in 2004. Our principal executive offices are located at 4 Maguire Road, Lexington, Massachusetts 02421 and our telephone number is (781) 761-7600. Our website is located at <http://www.epixpharma.com>. Our Corporate Code of Conduct and Ethics as well as our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and all amendments to these reports, which have been filed with the Securities and Exchange Commission, or SEC, are available to you free of charge through the Investor Relations section on our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC. We do not intend for the information contained in our website to be considered a part of this Form 10-K.

## **ITEM 1A. RISK FACTORS**

*We operate in a rapidly changing environment that involves a number of risks, some of which are beyond our control. This discussion highlights some of the risks which may affect future operating results. These are the risks and uncertainties we believe are most important for you to consider. Additional risks and uncertainties not presently known to us, which we currently deem immaterial or which are similar to those*

*faced by other companies in our industry or business in general, may also impair our business operations. If any of the following risks or uncertainties actually occurs, our business, financial condition and operating results would likely suffer.*

## **RISKS RELATED TO OUR BUSINESS**

***We anticipate future losses and may never become profitable.***

Our future financial results are uncertain. We have experienced significant losses since we commenced operations in 1992. Our accumulated net losses as of December 31, 2007 were approximately \$408.2 million. These losses have primarily resulted from expenses associated with our research and development activities, including preclinical studies and clinical trials, acquired in-process research and development from the merger with Predix and general and administrative expenses. We anticipate that our research and development expenses will remain significant in the future and we expect to incur losses over at least the next several years as we continue our research and development efforts, preclinical testing and clinical trials. In particular, we believe that we will be required to conduct additional clinical trials to obtain approval from the FDA for any of our therapeutic product candidates, which trials would be expensive and which could contribute to our continuing to incur losses.

As a result, we cannot predict when we will become profitable, if at all, and if we do, we may not remain profitable for any substantial period of time. If we fail to achieve profitability within the timeframe expected by investors, the market price of our common stock may decline and consequently our business may not be sustainable.

***We may need to raise additional funds necessary to fund our operations, and if we do not do so, we may not be able to implement our business plan.***

Since inception, we have funded our operations primarily through our public offerings of common stock, private sales of equity securities, debt financing, equipment lease financings, product development revenue, and royalty and license payments from our strategic partners. Although we believe that we have adequate funding to fund our operations through the first quarter of 2009, we may need to raise substantial additional funds for research, development and other expenses through equity or debt financings, strategic alliances or otherwise. Our future liquidity and capital requirements will depend upon numerous factors, including the following:

- the progress and scope of clinical trials;
- the timing and costs of filing future regulatory submissions;
- the timing and costs required to receive both U.S. and foreign governmental approvals;
- the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights;
- the extent to which our product candidates gain market acceptance;
- the timing and costs of product introductions;
- the extent of our ongoing and any new research and development programs;
- changes in our strategy or our planned activities;
- the costs of training physicians to become proficient with the use of our product candidates; and
- the costs of developing marketing and distribution capabilities.

If we raise additional funds through the issuance of equity or convertible debt securities, the percentage ownership of our stockholders could be significantly diluted, and these newly issued securities may have rights, preferences or privileges senior to those of existing stockholders. If we incur additional debt financing, a substantial portion of our operating cash flow may be dedicated to the payment of principal and interest on

such indebtedness, thus limiting funds available for our business activities. We cannot assure you that additional financing will be available on terms favorable to us, or at all. If adequate funds are not available or are not available on acceptable terms, when we desire them, our ability to fund our operations, take advantage of unanticipated opportunities or otherwise respond to competitive pressures would be significantly limited.

***We significantly increased our leverage as a result of the sale of 3.0% Convertible Senior Notes due 2024, and may be unable to repay, repurchase or redeem these notes if, and when, required.***

In connection with the sale of 3.0% Convertible Senior Notes due 2024, we have incurred indebtedness of \$100.0 million. Each \$1,000 of senior notes is convertible into 22.39 shares of our common stock representing a conversion price of approximately \$44.66 per share. Our ability to meet our debt service obligations will depend upon our future performance, which will be subject to regulatory approvals and sales of our products, as well as other financial and business factors affecting our operations, many of which are beyond our control. The amount of our indebtedness could, among other things:

- make it difficult for us to make payments on the notes;
- make it difficult for us to obtain financing for working capital, acquisitions or other purposes on favorable terms, if at all;
- make us more vulnerable to industry downturns and competitive pressures; and
- limit our flexibility in planning for, or reacting to changes in, our business.

In addition, although our 3.0% Convertible Senior Notes do not mature until 2024, noteholders may require us to repurchase these notes at par, plus accrued and unpaid interest, on June 15, 2011, 2014 and 2019 and upon certain other designated events under the notes, which include a change of control of us or termination of trading of our common stock on the NASDAQ Global Market. The definition of change in control set forth in the indenture governing the notes does not include certain mergers and similar transactions that are not deemed a change in control. While we believe that our merger with Predix did not constitute a change of control of us under the indenture, we cannot assure you that we will not become obligated to repurchase these notes, in whole or in part, as a result of the merger. Based on the current trading price of our common stock, we anticipate that in such event most, if not all, of the noteholders would tender their notes for repurchase. We may not have enough funds or be able to arrange for additional financing to repurchase the notes tendered by the holders upon a designated event or otherwise. Any failure to repurchase tendered notes would constitute an event of default under the indenture. If we are required to repurchase or redeem these notes prior to their maturity, whether as a result of the merger or otherwise, our financial position would be materially adversely affected and the anticipated benefits of the merger would be significantly diminished.

***A substantial portion of our future revenues will be dependent upon our agreements with GlaxoSmithKline, Amgen Inc. and Bayer Schering Pharma AG, Germany.***

We expect that a substantial portion of our future revenues will be dependent upon our collaboration agreements with GlaxoSmithKline and with Amgen Inc. The agreement with GlaxoSmithKline encompasses the development and commercialization of medicines targeting four G-protein coupled receptors, or GPCRs, for the treatment of a variety of diseases, including an option to license our 5-HT<sub>4</sub> partial agonist, PRX-03140, and other medicines arising from the four research programs. The agreement with Amgen encompasses the development and commercialization of products based on our preclinical compounds that modulate the 5-HT<sub>1D</sub> receptor and compounds and products that may be identified by or acquired by Amgen and that modulate the 5-HT<sub>1D</sub> receptor. We are dependent upon Bayer Schering Pharma AG, Germany to commercialize Vasovist, our lead imaging product candidate, in the United States and Europe. If these collaborators were to terminate their agreements with us, fail to meet their obligations or otherwise decrease their commitment there under, our future revenues could be materially adversely affected and the development and commercialization of our product candidates would be interrupted. In addition, if we do not achieve some or any of the development, regulatory and commercial milestones or if GlaxoSmithKline or Amgen does not achieve certain net sales thresholds, in each case, as set forth in the respective agreements, we will not fully realize the

expected benefits of the agreements. Further, the achievement of certain of the various milestones under our collaboration agreements with GlaxoSmithKline, Amgen and Bayer Schering Pharma AG, Germany will depend on factors that are outside of our control and most are not expected for several years, if at all. Moreover, our receipt of revenues under our agreements with these collaborators will be directly affected by the level of efforts of such collaborators and we cannot control whether they will devote sufficient resources to development or commercialization of the technology under their respective agreement or whether they will elect to pursue the development or commercialization of alternative products or services. For instance, Bayer Schering Pharma AG, Germany currently markets imaging agents for other technologies that will compete against Vasovist, and Bayer Schering Pharma AG, Germany will be responsible for setting the price of the product candidate worldwide. Accordingly, Bayer Schering Pharma AG, Germany may not set prices in a manner that maximizes revenues for us. Disagreements with our collaborators could delay or terminate the continued development and commercialization of the licensed products under our agreements or result in litigation, either of which could have a material adverse effect on our business, financial condition and results of operations overall. In addition, Bayer Schering Pharma AG, Germany was recently formed through the merger of Bayer AG and Schering AG. If the strategy of Bayer Schering Pharma AG, Germany differs from that of Schering AG's prior strategy with respect to the marketing of Vasovist, our expectations regarding the marketing of Vasovist could be negatively impacted, which could have a material adverse effect on our imaging business. If any of our agreements with GlaxoSmithKline, Amgen or Bayer Schering Pharma AG, Germany is terminated prior to expiration, we would be required to enter into other strategic relationships or find alternative ways of continuing our product development programs. We cannot assure you that we would be able to enter into similar agreements with other companies with sufficient product development capabilities to commercialize our product candidates, and our failure to do so could materially and adversely affect our ability to generate revenues.

***We have never had a commercially available product in the United States and we may never succeed in developing marketable products.***

We have never had any product candidates receive regulatory approval for commercial sale in the United States and do not expect to have any commercial therapeutic products available in the United States for at least the next several years, if at all. In September 2006, results from our pivotal Phase 3 clinical trial of our PRX-00023 product candidate for generalized anxiety disorder demonstrated that PRX-00023 did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to generalized anxiety disorder. Prior to obtaining results from this trial, PRX-00023 was our most advanced therapeutic drug candidate. Based on these trial results, however, we have discontinued our development efforts with respect to PRX-00023 in anxiety and currently are focusing our development efforts for this product candidate in depression. Although we commenced a Phase 2b clinical trial of PRX-00023 for the treatment of depression in March 2007, PRX-00023 will require significant further testing for that indication. In addition, although our Vasovist imaging product has been approved for commercial sale, and is currently being marketed, in certain countries outside of the United States, we have not obtained approval of Vasovist in the United States and do not expect any significant income or royalties as a result of sales of Vasovist outside of the United States for the foreseeable future. The approval of Vasovist by the FDA is subject to continued uncertainty and we may never obtain regulatory approval to market Vasovist in the United States.

In addition to PRX-00023 and Vasovist, each of our other clinical-stage drug candidates in the United States require additional clinical studies: PRX-08066 for the treatment of two types of pulmonary hypertension — pulmonary hypertension associated with chronic obstructive pulmonary disease and pulmonary arterial hypertension; PRX-03140 for the treatment of Alzheimer's disease; and PRX-07034 for the treatment of cognitive impairment. Prior to the initiation of our Phase 2 clinical trial, PRX-08066 had never been tested in patients with pulmonary hypertension associated with chronic obstructive pulmonary disease and has never been tested in patients with primary pulmonary arterial hypertension. PRX-07034 has only been tested in obese but otherwise healthy subjects and has never been tested in subjects with cognitive impairment. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in early-stage clinical development. For example, Sanofi-Aventis discontinued the development of its product candidate for the treatment of

Alzheimer's disease designed to target the 5-HT<sub>4</sub> protein receptor due to lack of efficacy. This compound is believed to have the same mechanism of action as PRX-03140, was more advanced in clinical development and was more potent in vitro assays. Accordingly, the results from the completed and ongoing studies and trials for our product candidates may not be predictive of the results we may obtain in later-stage clinical trials. If we are unable to develop one or more marketable products in the United States, or elsewhere, our results of operations, business and future prospects would be materially harmed.

***We have never generated positive cash flow, and if we fail to generate revenue, it will have a material adverse effect on our business.***

To date, we have received revenues from payments made under licensing, royalty arrangements and product development and marketing agreements with strategic collaborators. In particular, our revenue for the twelve months ended December 31, 2007 was \$14.9 million and consisted of \$10.2 million of product development revenue from Bayer Schering Pharma AG, Germany, GlaxoSmithKline and CFFT, \$1.0 million of royalty revenue related to the Bracco and Bayer Schering Pharma AG, Germany agreements, and \$3.7 million of license fee revenue related to the Bayer Schering Pharma AG, Germany, Amgen, Covidien, GlaxoSmithKline and CFFT agreements. In addition to these sources of revenue, we have financed our operations to date through public stock and debt offerings, private sales of equity securities and equipment lease financings.

Although we believe that we are currently in compliance with the terms of our collaboration and licensing agreements, the revenues derived from them are subject to fluctuation in timing and amount. We may not receive anticipated revenue under our existing collaboration or licensing agreements, these agreements may be subject to disputes and, additionally, these agreements may be terminated upon certain circumstances. Therefore, to achieve profitable and sustainable operations, we, alone or with others, must successfully develop, obtain regulatory approval for, introduce, market and sell products. We may not receive revenue from the sale of any of our product candidates for the next several years because we, and our partners, may not:

- successfully complete our product development efforts;
- obtain required regulatory approvals in a timely manner, if at all;
- manufacture our product candidates at an acceptable cost and with acceptable quality; or
- successfully market any approved products.

As a result, we may never generate revenues from sales of our product candidates and our failure to generate positive cash flow could cause our business to fail.

***We depend on our strategic collaborators for support in product development and the regulatory approval process for our product candidates and, if approved, for product marketing.***

Our product development programs and potential regulatory approval and commercialization of our product candidates will require substantial additional cash to fund expenses. Our strategy includes collaborating with leading pharmaceutical, biotechnology or other companies to assist us in further developing and potentially commercializing our product candidates requiring large commercial sales and marketing infrastructures. We may also seek to enter into such collaborations for our other product candidates, especially for target indications in which the potential collaborator has particular expertise or that involve a large, primary care market that must be served by large sales and marketing organizations. In addition, we depend, and expect to continue to depend, on strategic collaborators for support in a variety of other activities including manufacturing, marketing and distribution of our product candidates in the United States and abroad, if the FDA and corresponding foreign agencies approve our product candidates for marketing. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time-consuming to negotiate and document.

We may not be able to enter into any such collaboration on terms that are acceptable to us, or at all. If that were to occur, we may have to curtail the development of a particular product candidate, reduce or delay one or more of our development programs or potential commercialization, or increase our expenditures and undertake development or commercialization activities at our own expense. For instance, on July 12, 2006, Bayer Schering

Pharma AG, Germany notified us that it decided not to exercise its option to exclusively license EP-2104R, our imaging agent that has completed a Phase 2 clinical trial. As a result, we discontinued the development of EP-2104R. If we elect to increase our expenditures to fund development, potential regulatory approval or commercialization activities on our own, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not obtain sufficient funds, we will not be able to complete clinical development of our product candidates or bring our product candidates to market. Further, our receipt of revenues from strategic alliances is affected by the level of efforts of our collaborators. Our collaborators may not devote the resources necessary to complete development and commence marketing of a product candidate in their respective territories, or they may not successfully market product candidates.

***We rely on third-parties to conduct our clinical trials, and those third-parties may not perform satisfactorily, including failing to maintain adequate diligence in the conduct of our trials and failing to meet established deadlines for the completion of such trials.***

We do not have the ability to independently conduct clinical trials for our product candidates, and we rely on third-parties such as contract research organizations, medical institutions and clinical investigators to enroll qualified patients and conduct our clinical trials. Our reliance on these third-parties for clinical development activities reduces our control over these activities. Accordingly, these third-party contractors may not complete activities on schedule, or may not conduct our clinical trials in accordance with regulatory requirements or our trial design. Our reliance on third-parties that we do not control does not relieve us of our requirement to prepare, and ensure our compliance with, various procedures required under good clinical practices, even though third-party contract research organizations have prepared and are complying with their own, comparable procedures. If these third-parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third-parties need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our preclinical development activities or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, our product candidates. In addition, if our contract research organizations and other similar entities with which we are working do not successfully carry out their contractual duties or meet expected deadlines, we may be required to replace them. For example, in January 2008, we had to cease doing business with one of our third-party contract research organizations as a result of errors in the trial results from our Phase 2a clinical trial of PRX-03140 which were provided by such third-party and publicly reported by us. Although we believe that there are other third-party contractors we could engage to continue these activities, it may result in a delay of the affected trial. In addition, our failure to accurately report study data, whether as a result of a failure by a third-party or otherwise, could harm our reputation and subject us to liability.

***If clinical trials for our product candidates are prolonged or delayed, we may be unable to commercialize our product candidates on a timely basis, which would require us to incur additional costs and delay our receipt of any revenue from potential product sales.***

We may encounter problems with our completed, ongoing or planned clinical trials for our product candidates that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our ongoing and planned clinical trials for our product candidates and negatively impact our ability to obtain regulatory approval or enter into collaborations for, or market or sell, a particular product candidate, including any of our current clinical-stage product candidates:

- conditions imposed on us by the FDA or any foreign regulatory authority regarding the scope or design of our clinical trials;
- delays in obtaining, or our inability to obtain, required approvals from institutional review boards or other reviewing entities at clinical sites selected for participation in our clinical trials;
- delay in developing a clinical dosage form, insufficient supply or deficient quality of our product candidates or other materials necessary to conduct our clinical trials;

- negative or inconclusive results from clinical trials, or results that are inconsistent with earlier results, that necessitate additional clinical study;
- serious and/or unexpected product-related side effects experienced by subjects in clinical trials; or
- failure of our third-party contractors or our investigators to comply with regulatory requirements or otherwise meet their contractual obligations to us in a timely manner.

Regulatory authorities, clinical investigators, institutional review boards, data safety monitoring boards and the hospitals at which our clinical trials are conducted all have the power to stop our clinical trials prior to completion. Our clinical trials for our product candidates may not begin as planned, may need to be restructured, and may not be completed on schedule, if at all. For example, in September 2001, after discussions with the FDA, we expanded our initial target indication for Vasovist from one specific body region, the aortoiliac region, to a broader indication that included the entire body's vascular system, except for the heart. This expansion required us to add two new clinical trials to our then existing Phase 3 clinical trial program. This change to the Phase 3 clinical trial program and the associated delay in the startup of new clinical centers resulted in an approximate 15-month delay in our NDA submission and an increase in costs associated with the program. Delays in clinical trials may result in increased development costs for our product candidates. In addition, if our clinical trials for our product candidates are delayed, our competitors may be able to bring product candidates to market before we do and the commercial viability of our product candidates could be significantly reduced.

In addition, the number and complexity of clinical trials needed to achieve regulatory approval for our therapeutic drug candidates, including but not limited to PRX-00023, our product candidate for the treatment of depression, and PRX-03140, our product candidate for the treatment of Alzheimer's disease, could be significant. Achieving primary efficacy endpoints in depression and anxiety trials is difficult due to the significant placebo effect commonly observed in trials in these patient populations. For example, results from our completed Phase 3 clinical trial of PRX-00023 demonstrated that the product candidate did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to generalized anxiety disorder. Based on these results, we have discontinued our development efforts with respect to PRX-00023 in anxiety and are focusing our efforts with respect to PRX-00023 in depression. In addition, we must also submit the results of a two-year carcinogenicity study of PRX-00023 prior to its approval. We have not yet initiated this study and intend to conduct this study prior to submitting an NDA to the FDA. If the clinical development of PRX-00023 is delayed as a result of these matters, additional requirements set forth by the FDA, including requirements related to confirming the correct dose for PRX-00023, or otherwise, the time and cost of the development of PRX-00023 could increase significantly.

***If we are unsuccessful in our appeal process for Vasovist with the FDA, we may never obtain approval to market and sell Vasovist in the United States and our revenues will be materially harmed.***

Vasovist has not been approved for marketing and sale in the United States by the FDA. In connection with a new drug application, or NDA, that we submitted for Vasovist in December 2003, we received an approvable letter from the FDA in January 2005 in which the FDA requested additional clinical trials prior to approval. In May 2005, we submitted a response to the FDA approvable letter, which was accepted by the FDA as a complete response in June 2005. In November 2005, the FDA provided us with a second approvable letter which indicated that at least one additional clinical trial and a re-read of images obtained in certain previously completed Phase 3 trials will be necessary before the FDA could approve Vasovist. After considering the parameters of the additional clinical trials requested by the FDA, we filed a formal appeal with the FDA asking the FDA to approve Vasovist and to utilize an advisory committee as part of the appeal process. In August 2006, the FDA denied our appeal and suggested that we conduct two new clinical trials for Vasovist. In February 2007, we filed our second formal appeal with the FDA asking the FDA to approve Vasovist and to utilize an advisory committee as part of the appeal process. On June 15, 2007, we received a letter from the FDA denying our second formal appeal, but indicated that a blinded re-read, or reanalysis, of the images obtained in our previously completed Phase 3 clinical trials of Vasovist could provide the potential evidence to support approval of Vasovist if the results of the re-read are positive. In January 2008, we initiated

the re-read of the images obtained in prior Phase 3 studies. The approval, timeliness of approval and labeling of Vasovist, however, remain subject to significant uncertainties related to a number of factors, including:

- obtaining positive results of such a re-read of images by a new group of radiologists; and
- the FDA's review process and conclusions regarding any additional Vasovist regulatory submissions.

We cannot assure you that the blinded re-read process will be successful or that the FDA will approve Vasovist upon the resubmission of the NDA if the re-read is successful. If the FDA does not approve Vasovist, we will not receive revenues based on sales of Vasovist in the United States.

***If we are unable to obtain required regulatory approval of our therapeutic product candidates, we will be unable to market and sell our therapeutic product candidates and our business will be materially harmed.***

Our existing therapeutic product candidates and any other product candidates we may discover or acquire and seek to commercialize are subject to extensive regulation by the FDA and similar regulatory agencies in other countries relating to development, clinical trials, manufacturing and commercialization. In the United States and in many foreign jurisdictions, rigorous preclinical testing and clinical trials and an extensive regulatory review process must be successfully completed before a new product candidate can be sold. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. The time required to obtain approval by the FDA is unpredictable but typically exceeds five years following the commencement of clinical trials, depending upon many factors, including the complexity of the product candidate. We initiated clinical trials for PRX-08066, PRX-00023, PRX-03140 and PRX-07034 in May 2005, February 2004, December 2004 and June 2006, respectively, and thus far, these therapeutic product candidates have been studied in only a small number of patients. Early-stage clinical trials in small numbers of patients are often not predictive of results in later-stage clinical trials with a larger and more diverse patient population. Even product candidates with favorable results in late-stage pivotal clinical trials may fail to get approved for commercialization for many reasons, including:

- our failure to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for a particular indication;
- our inability to demonstrate that a product candidate's benefits outweigh its risks;
- our inability to demonstrate that the product candidate presents a significant advantage over existing therapies;
- the FDA's or comparable foreign regulatory authorities' disagreement with the manner in which we and our collaborators interpret the data from preclinical studies or clinical trials;
- the FDA's or comparable foreign regulatory authorities' failure to approve our manufacturing processes or facilities or the processes or facilities of our collaborators; or
- a change in the approval policies or regulations of the FDA or comparable foreign regulatory authorities.

The relevant regulatory authorities may not approve any of our applications for marketing authorization relating to any of our product candidates, or additional applications for or variations to marketing authorizations that we may make in the future as to these or other product candidates. Among other things, we have had only limited experience in preparing applications and obtaining regulatory approvals. If approval is granted, it may be subject to limitations on the indicated uses for which the product candidate may be marketed or contain requirements for costly post-marketing testing and surveillance to monitor safety or efficacy of the product candidate. If approval of an application to market product candidates is not granted on a timely basis or at all, or if we are unable to maintain our approval, our business may be materially harmed. It is possible that none of our product candidates or any other product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us to begin selling them, which would materially harm our business.

***Our clinical trials may not yield results that will enable us to obtain regulatory approval for our product candidates.***

We will only receive regulatory approval to commercialize a product candidate if we can demonstrate to the satisfaction of the FDA or the applicable foreign regulatory agency, in well-designed and conducted clinical trials, that the product candidate is safe and effective and otherwise meets the appropriate standards required for approval for a particular indication. Clinical trials are lengthy, complex and extremely expensive processes with uncertain results. For example, results from our completed Phase 3 clinical trial of PRX-00023 in generalized anxiety disorder, which was designed to evaluate the efficacy of PRX-00023 as measured by the change from baseline in the Hamilton Rating Scale for Anxiety compared to placebo, demonstrated that PRX-00023 did not achieve a statistically significant improvement over placebo for the primary endpoint with respect to generalized anxiety disorder. Based on these results, we have discontinued our development efforts of PRX-00023 in anxiety. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals for our product candidates, including filing and prosecuting the applications necessary to gain approval by the FDA. Our NDA for Vasovist has not been, and may never be, approved by the FDA and we have not submitted an NDA to the FDA for any of our other product candidates. This limited experience may result in longer regulatory processes in connection with our efforts to obtain approval of our product candidates. With respect to both our current product candidates in human clinical trials and our research product candidates which may be suitable for testing in human clinical trials at some point in the future, we face risks including that:

- the product candidate may not prove to be safe and efficacious;
- the dosage form of the product candidate may not deliver reproducible amounts of product to patients;
- patients may die or suffer other adverse effects for reasons that may or may not be related to the product candidate being tested;
- the results of later-stage clinical trials may not confirm the positive results of earlier trials;
- the results may not meet the level of statistical significance required by the FDA or other regulatory agencies for approval; and
- the FDA or other regulatory agencies may require additional or expanded trials.

Of the large number of product candidates in development, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization. If we fail to demonstrate the safety and efficacy of our product candidates, we will not be able to obtain the required regulatory approvals to commercialize these product candidates. The results from preclinical testing of a product candidate that is under development may not be predictive of results that will be obtained in human clinical trials. In addition, the results of early human clinical trials may not be predictive of results that will be obtained in larger scale, advanced-stage clinical trials. Our current product candidates and any other product candidates we may seek to develop in the future may never complete the clinical testing necessary to obtain the appropriate regulatory approvals for us to begin selling them.

***Gadolinium-based imaging agents, such as Vasovist, may cause adverse side effects which could limit our ability to receive approval for these product candidates and our ability to effectively market these product candidates, if approved.***

Vasovist is a contrast drug that contains gadolinium. In May 2006, the Danish Medicines Agency announced that it was investigating a possible link between the use of Omniscan, an imaging agent containing gadolinium, and the development of a very rare skin disease, nephrogenic systemic fibrosis (NSF), in 25 patients with severely impaired renal function who had been administered the imaging agent. Further investigations with respect to all MRI contrast media containing gadolinium revealed that NSF also has developed following the administration of two other gadolinium-containing agents (OptiMARK and Magnevist). It also has been reported that NSF may affect internal anatomy as well as the skin. Although a causative relationship between gadolinium-containing agents and NSF has not been definitively established, evidence is

increasing. By May 2007, the use of Omniscan and Magnevist had been contraindicated in patients with severe renal impairment by the EMEA (European Medicines Agency). For all other gadolinium-containing contrast agents, safety warnings about the potential for NSF in patients with severe renal impairment were added to the product information. By May 2007, the FDA requested that manufacturers of all gadolinium-containing agents add a Boxed Warning and new Warning section that describes the risk of NSF because it is impossible at present to definitively determine whether the extent of risks for developing NSF are the same for all gadolinium-containing agents. We are also aware of ongoing litigation in the United States relating to the use of imaging agents containing gadolinium. To date, over 250 cases of NSF have been reported world-wide. Although we have reviewed our safety databases for Vasovist and have found no instances of this rare disease, our databases may be too small to show such an effect, if it exists. In the event gadolinium-based imaging agents such as Vasovist are directly linked to this very rare disease or other unanticipated side effects, such safety concerns could have a material adverse effect on our ability to obtain marketing approval for Vasovist or any such approval for use may be revoked. Moreover, even if a direct link is not conclusively established, any safety concerns regarding gadolinium-based imaging agents could also materially harm our and our partners' ability to successfully market Vasovist.

***If we encounter difficulties enrolling subjects in our clinical trials for our product candidates, or subjects drop out of trials in progress for our product candidates, our trials could be delayed or otherwise adversely affected.***

The timing of completion of clinical trials is dependent in part upon the rate of enrollment of patients. Patient accrual is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the existence of competitive clinical trials, and the availability of alternative treatments. Delays in planned patient enrollment may result in increased costs and prolonged clinical development. In addition, patients may withdraw from a clinical trial for a variety of reasons. If we fail to accrue and maintain the number of patients into one of our clinical trials for which the clinical trial was designed, the statistical power of that clinical trial may be reduced which would make it harder to demonstrate that the product candidate being tested in such clinical trial are safe and effective. We may not be able to enroll a sufficient number of qualified patients in a timely or cost-effective manner. For example, we experienced difficulty in enrolling healthy elderly volunteers in our Phase 1 clinical trial for PRX-03140. Any future delays in patient enrollment could result in increased costs and longer development times. Enrollment of patients in our clinical trials for our product candidates is affected by many factors, including:

- the limited size of the patient population and the availability of commercial products for certain target indications, including pulmonary arterial hypertension and pulmonary hypertension associated with chronic obstructive pulmonary disease;
- the nature and design of the trial protocol;
- the proximity of patients to clinical sites;
- the availability of other effective treatments for the relevant disease (whether approved or experimental);
- the eligibility criteria for enrollment in our clinical trials;
- perceived risks and benefits of the product candidate under study; and
- competing studies or trials.

In addition, the FDA could require us to conduct clinical trials with a larger number of subjects than we have projected for any of our product candidates. If we have difficulty enrolling or retaining a sufficient number of patients to participate and complete our clinical trials for our product candidates as planned, we may need to delay or terminate ongoing or planned clinical trials. Delays in enrolling patients in these clinical trials or the withdrawal of subjects enrolled in these clinical trials would adversely affect our ability to develop and seek approval for our product candidates, could delay or eliminate our ability to generate product candidates and revenue and could impose significant additional costs on us.

***Our therapeutic product candidates are currently unformulated.***

All of our therapeutic product candidates, including PRX-08066, PRX-00023, PRX-03140 and PRX-07034, are currently unformulated. The lack of an optimized and commercially-viable formulation during clinical trials may have a significant impact in the overall development and commercialization of these therapeutic product candidates, including:

- the current dosage may not provide reproducible amounts of product;
- the pharmaceutical development of a commercially viable formulation may add significant cost and time to our clinical development programs for therapeutics;
- additional trials may be required if the new formulation is not bioequivalent to formulations already used in clinical trials;
- future clinical trials may be delayed in order to identify, develop, optimize, manufacture and certify a commercially viable formulation; and
- regulatory filings, and/or commercial launch may be delayed due to the lack of a commercial process for cGMP manufacturing of the new formulation.

The occurrence of any of the foregoing could materially harm our business.

***Our prior stock option practices may result in significant liability.***

Prior to the change in our senior management in connection with the merger with Predix Pharmaceuticals Holdings, Inc. on August 16, 2006, certain employees, including certain of our former senior management, participated in retrospective date selection for the grant of certain stock options and re-priced, as defined by financial accounting standards, certain options during the period from 1997 through 2005. Accordingly, our audit committee concluded that, pursuant to Accounting Principles Board No. 25 (APB 25) and related interpretations, the accounting measurement date for the stock option grants for which those members of our former senior management had retrospectively selected grant dates for certain grants awarded between February 1997 and February 2004, covering options to purchase approximately 1.4 million shares of our common stock, differed from the measurement dates previously used for such stock awards. In addition, we determined that certain of our former senior management re-priced, as defined by financial accounting standards, approximately 0.9 million stock options awarded during the period between June 1999 and March 2005, and we identified approximately 0.1 million options in which other dating errors resulted in stock options with grant dates that failed to meet the measurement date criteria of APB 25. As a result, we applied revised measurement dates to the option grants with administrative errors and option grants for which certain of our former senior management retrospectively selected grant dates, and, for options that were re-priced, as defined by financial accounting standards, we revised our accounting for such re-priced awards from accounting for the grants as fixed awards to accounting for the grants as variable awards. As a result of these adjustments, in connection with the filing of our 2006 Form 10-K, we restated our historical financial statements for the years 1997 through 2005 to record an aggregate of \$7.4 million in additional stock-based compensation expense for those periods. In addition, we accrued payroll tax expense of approximately \$0.9 million relating to employer and employee payroll taxes, interest and penalties we estimate we will owe as a result of the modifications to exercised options previously considered incentive stock options that should have been taxed as non-qualified stock options. Our historical stock option practices and the restatement of our prior financial statements expose us to greater risks associated with litigation and regulatory proceedings. The Securities and Exchange Commission has advised us that it has commenced an informal investigation regarding our stock option grants. We are cooperating with that investigation. In the event of any litigation or regulatory proceeding involving a finding or assertion by the Securities and Exchange Commission, other federal or state governmental agencies, or any third-party that our past stock option practices violated the federal securities laws or other laws, we may be required to pay fines, penalties or other amounts, may be subject to other remedies or remedial actions, and/or may be required to further restate prior period financial statements or adjust current period financial statements. In addition, considerable legal and accounting

expenses related to these matters have been incurred to date and significant expenditures may be incurred in the future.

***Failure to comply with foreign regulatory requirements governing human clinical trials and marketing approval for our product candidates could prevent us from selling our product candidates in foreign markets, which may adversely affect our operating results and financial condition.***

The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement for marketing our product candidates outside the United States vary greatly from country to country and may require additional testing. We have no experience in obtaining regulatory approvals for any of our product candidates. Although the use of Vasovist has been approved in the European Union, as well as Canada, Iceland, Norway, Switzerland, Turkey and Australia, Bayer Schering Pharma AG, Germany is responsible for obtaining foreign regulatory approvals for Vasovist. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA. Failure to comply with these regulatory requirements or obtain required approvals could impair our ability to develop foreign markets for our product candidates.

***Our product candidates will remain subject to ongoing regulatory requirements even if they receive marketing approval, and if we fail to comply with requirements, we could lose these approvals and the sale of any approved commercial products could be temporarily or permanently suspended.***

Even if we receive regulatory approval to market a particular product candidate, the product will remain subject to extensive regulatory requirements, including requirements relating to manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping. In addition, as clinical experience with a product expands after approval because it is typically used by a greater number of patients after approval than during clinical trials, side effects and other problems may be observed after approval that were not seen or anticipated during pre-approval clinical trials. We are required to maintain pharmacovigilance systems for collecting and reporting information concerning suspected adverse reactions to our product candidates. In response to pharmacovigilance reports, regulatory authorities may initiate proceedings to revise the prescribing information for our product candidates or to suspend or revoke our marketing authorizations. Procedural safeguards are often limited, and marketing authorizations can be suspended with little or no advance notice. Both before and after approval of a product, quality control and manufacturing procedures must conform to cGMP. Regulatory authorities, including the European Medicines Agency, or EMEA, and the FDA, periodically inspect manufacturing facilities to assess compliance with cGMP. Accordingly, we and our contract manufacturers will need to continue to expend time, funds, and effort in the area of production and quality control to maintain cGMP compliance. If we fail to comply with the regulatory requirements of the FDA, the EMEA and other applicable U.S. and foreign regulatory authorities or previously unknown problems with any approved commercial products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions or other setbacks, including:

- restrictions on the products, manufacturers or manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- import bans;
- product recalls and related publicity requirements;

- unanticipated expenditures;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new products or supplements to approved applications.

The imposition on us of any of the foregoing could materially harm our results of operations. In addition to regulations adopted by the EMEA, the FDA, and other foreign regulatory authorities, we are also subject to regulation under the Occupational Safety and Health Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, and other federal, state, and local regulations.

***We are focusing our therapeutic product discovery and development efforts on G-Protein Coupled Receptor and ion channel-targeted product candidates, which have historically had a high incidence of adverse side effects.***

Despite commercial success, many G-Protein Coupled Receptor, or GPCR, and ion channel-targeted products have been associated with a high incidence of adverse side effects due in part to poor selectivity in binding to their target protein, resulting in binding to other “off-target” proteins. We believe we are designing our therapeutic product candidates to be highly selective and as a result to have a favorable side-effect profile. However, all of our therapeutic product candidates are in early stages of development, and although our clinical therapeutic product candidates have to date exhibited acceptable side-effect profiles in clinical trials in a limited number of subjects, we cannot assure you that these results will be repeated in larger-scale trials. If serious side effects occur in later-stage clinical trials of our therapeutic product candidates, we may not receive regulatory approval to commercialize them. Even if any of our therapeutic product candidates receive regulatory approval, if they do not exhibit a more favorable side-effect profile than existing therapies, our competitive position could be substantially diminished.

***The application of our in silico therapeutic product discovery technology and approach may be limited to a subset of therapeutically useful proteins, which may reduce the opportunities to develop and commercialize product candidates against other important therapeutic targets.***

To date, our technology and approach has generated clinical therapeutic product candidates, including PRX-08066, PRX-00023, PRX-03140 and PRX-07034, which mimic the activity of a small molecule, serotonin, within a class of GPCR proteins known as serotonergic receptors. The activity is achieved through binding of the ligand, serotonin, to a particular region of the protein that spans the cell membrane. These GPCRs and mechanisms of interaction represent a small subset of all known therapeutically-relevant GPCRs. Ion channels can consist of multiple protein subunits that have complex and subtle mechanisms of activation and inactivation. Therefore, it may be difficult to apply our proprietary product discovery technology to small-molecule ion channel targets.

Although we believe that the in silico technology platform can be utilized and developed to discover such small molecules, we cannot ensure that our in silico technology and approach will generate clinical candidates for all GPCRs and ion channels that are important targets for therapeutic intervention.

***Our competitors may develop products that are less expensive, safer or more effective, which may diminish or eliminate the commercial success of any future products that we may commercialize.***

Competition in the pharmaceutical and biotechnology industries is intense and expected to increase. We face competition from pharmaceutical and biotechnology companies, as well as numerous academic and research institutions and governmental agencies engaged in product discovery activities or funding, both in the United States and abroad. Some of these competitors have therapeutic products or are pursuing the development of therapeutic product candidates that target the same diseases and conditions that are the focus of our clinical-stage therapeutic product candidates, including the following:

- **PRX-00023.** If approved, PRX-00023, the product candidate we are developing for the treatment of depression, may compete with approved products from such pharmaceutical companies as Forest

Laboratories, Inc., GlaxoSmithKline plc, Eli Lilly & Co., Pfizer Inc. and Wyeth, and may compete with several therapeutic product candidates in clinical development from other companies, including Sanofi-Aventis. We believe that there are over 60 therapeutic product candidates in clinical trials or that have been submitted for approval for the treatment of depression.

- *PRX-03140.* If approved, PRX-03140, the drug candidate we are developing for the treatment of Alzheimer's disease, may compete with approved products from such pharmaceutical companies as Forest Laboratories, Inc., Johnson & Johnson, Novartis AG and Pfizer, Inc., and may compete with drug candidates in clinical development from other companies, including Myriad Genetics, Inc., GlaxoSmithKline plc and Neurochem Inc. We are studying PRX-03140 both as monotherapy and in combination with approved products, such as Aricept which is marketed by Pfizer Inc. We believe that there are over 70 therapeutic product candidates in clinical trials for the treatment of Alzheimer's disease.
- *PRX-08066.* If approved, PRX-08066, the drug candidate we are developing for the treatment of pulmonary arterial hypertension (PAH), may compete with approved products from such pharmaceutical companies as Actelion Pharmaceuticals Ltd., GlaxoSmithKline plc, Pfizer Inc., Gilead Sciences Inc., and United Therapeutics Corporation, and may compete with drug candidates in clinical development by other companies, such as Encysive Pharmaceuticals Inc. and Bayer Schering Pharma AG. We believe that there are approximately ten therapeutic product candidates in clinical trials or that have been submitted for approval for the treatment of pulmonary arterial hypertension and/or pulmonary hypertension associated with chronic obstructive pulmonary disease.
- *PRX-07034.* If approved for the treatment of cognitive impairment (associated with schizophrenia or Alzheimer's disease), PRX-07034 may compete with approved products from such pharmaceutical companies as Forest Laboratories, Johnson & Johnson, Novartis AG and Pfizer, Inc., and may compete with several therapeutic product candidates in clinical development from other companies, including GlaxoSmithKline plc, AstraZeneca and Memory Pharmaceuticals Corp. We believe that there are over 60 therapeutic product candidates in clinical trials for the treatment of cognitive impairment in association with schizophrenia. If approved for the treatment of obesity, PRX-07034 may compete with approved products from such pharmaceutical companies as Abbott Laboratories and Roche Holding Ltd., and may compete with several therapeutic product candidates in clinical development by other companies, such as Sanofi-Aventis and Arena Pharmaceuticals, Inc. We believe that there are over 40 therapeutic product candidates in clinical trials for the treatment of obesity.

We expect that many patents covering commercial therapeutic products for these indications will expire in the next four to nine years, which will result in greater competition in these indications resulting from companies producing generic versions of the commercial products. Many of our competitors have therapeutic products that have been approved or are in advanced development and may develop superior technologies or methods to identify and validate therapeutic product targets and to discover novel small-molecule products. Our competitors may also develop alternative therapies that could further limit the market for any therapeutic products that we may develop.

In addition, there are a number of general use MRI agents approved for marketing in the United States, and in certain foreign markets that, if used or developed for magnetic resonance angiography, are likely to compete with Vasovist. Such products include Magnevist and Gadovist by Bayer Schering Pharma AG, Germany, Dotarem by Guerbet, S.A., Omniscan by GE Healthcare, ProHance and MultiHance by Bracco and OptiMARK by Covidien Ltd. We are aware of five agents under clinical development that have been or are being evaluated for use in magnetic resonance angiography: Bayer Schering Pharma AG, Germany's Gadomer and SHU555C, Guerbet, S.A.'s Vistarem, Bracco's B-22956/1, Ferropharm GmbH's Code VSOP-C184, and Advanced Magnetics Inc. Ferumoxylol. Moreover, there are several well-established medical imaging methods that currently compete and will continue to compete with MRI, including digital subtraction angiography, which is an improved form of X-ray angiography, computed tomography angiography, nuclear medicine and ultrasound, and there are companies that are actively developing the capabilities of these competing methods to enhance their effectiveness in vascular system imaging.

We cannot assure you that our competitors will not succeed in the future in developing therapeutic or imaging products that are more effective than any that we are developing. We believe that our ability to compete in developing commercial products depends on a number of factors, including the success and timeliness with which we complete FDA trials, the breadth of applications, if any, for which our product candidates receive approval, and the effectiveness, cost, safety and ease of use of our product candidates in comparison to the products of our competitors. In addition, these companies may be more successful than we are in developing, manufacturing and marketing their imaging products. In addition, many of our competitors and their collaborators have substantially greater capital, research and development resources, manufacturing, sales and marketing experience and capabilities. Smaller companies also may prove to be significant competitors, particularly through proprietary research discoveries and collaboration arrangements with large pharmaceutical and established biotechnology companies. Our competitors, either alone or with their collaborators, may succeed in developing products that are more effective, safer, more affordable or more easily administered than our product candidates and may achieve patent protection or commercialize product candidates sooner than us. Any inability to compete successfully on our part will have a materially adverse impact on our business and operating results.

***If the market does not accept our technology and product candidates, we may not generate sufficient revenues to achieve or maintain profitability.***

The commercial success of our product candidates, even if approved for marketing by the FDA and corresponding foreign agencies, depends on their acceptance by the medical community and third-party payors as clinically useful, cost-effective and safe. Market acceptance, and thus sales of our products, will depend on several factors, including:

- safety;
- cost-effectiveness relative to alternative therapies, methods or products;
- availability of third-party reimbursement;
- ease of administration;
- clinical efficacy; and
- availability of competitive products.

If any of our product candidates, when and if commercialized, do not achieve market acceptance, we may not generate sufficient revenues to achieve or maintain profitability.

In addition, market acceptance of our imaging product candidate will also depend on our ability and that of our strategic partners to educate the medical community and third-party payors about the benefits of diagnostic imaging with Vasovist-enhanced magnetic resonance angiography compared to imaging with other technologies. While we believe that contrast agents are currently used in an estimated 25% to 35% of all MRI exams, there are no MRI agents approved by the FDA for vascular imaging. Furthermore, clinical use of magnetic resonance angiography has been limited and use of magnetic resonance angiography for some vascular disease imaging has occurred mainly in research and academic centers. Vasovist represents a new approach to imaging the non-coronary vascular system, and market acceptance both of magnetic resonance angiography as an appropriate imaging technique for the non-coronary vascular system, and of Vasovist, is critical to our success.

***We may not be able to keep up with the rapid technological change in the biotechnology and pharmaceutical industries, which could make any of our future approved therapeutic products obsolete and reduce our revenue.***

Biotechnology and related pharmaceutical technologies have undergone and continue to be subject to rapid and significant change. Our future will depend in large part on our ability to maintain a competitive position with respect to these technologies. We believe that our proprietary therapeutic product discovery technology and approach enables structure-based discovery and optimization of certain GPCR and ion

channel-targeted drug candidates. However, our competitors may render our technologies obsolete by advances in existing GPCR and ion channel-targeted drug discovery approaches or the development of new or different approaches. In addition, any future therapeutic products that we develop, including our clinical-stage therapeutic product candidates, PRX-08066, PRX-00023, PRX-03140 and PRX-07034, may become obsolete before we recover expenses incurred in developing those therapeutic product candidates, which may require us to raise additional funds to continue our operations.

***We are currently focusing our imaging development efforts primarily on Vasovist and will have limited prospects for successful imaging operations if it does not prove successful.***

Since the merger with Predix, we are focusing our imaging development efforts on our lead imaging product candidate, Vasovist. Accordingly, we have decided to cease work on our research projects related to the development of EP-2104R. We are no longer allocating resources to any imaging research or clinical programs other than the efforts required to continue to pursue FDA approval of Vasovist. Our efforts may not lead to commercially successful imaging products for a number of reasons, including the inability to be proven safe and effective in clinical trials, the lack of regulatory approvals or obtaining regulatory approvals that are narrower than we seek, inadequate financial resources to complete the development and commercialization of our imaging product candidates or their lack of acceptance in the marketplace.

***Our product candidates require significant biological testing, preclinical testing, manufacturing and pharmaceutical development expertise and investment. We rely primarily on external partners to complete these activities.***

We have limited in-house biological and preclinical testing capabilities. Therefore, we rely heavily on third-parties to perform in vitro potency, in vivo functional efficacy, animal toxicology and pharmacokinetics testing prior to advancing our product candidates into clinical trials. We also do not have internal expertise to formulate our therapeutic product candidates. In addition, we do not have, nor do we currently have plans to develop, full-scale manufacturing capability for any of our product candidates, including Vasovist. We currently rely on Aptuit, Inc. and Thermo Fisher Scientific Inc. for our therapeutic drug product manufacturing and testing, and on Aptuit, Inc. and Johnson Matthey Pharma Services for the manufacture and testing of our active therapeutic pharmaceutical ingredients. Although we believe that we could replace these suppliers on commercially reasonable terms, if any of these third-parties fail to fulfill their obligations to us or do not successfully complete the testing in a timely or acceptable manner, our therapeutic product development efforts could be negatively impacted and/or delayed. We rely on Covidien as the primary manufacturer of Vasovist for any future human clinical trials and commercial use. Together with Bayer Schering Pharma AG, Germany, we are considering alternative manufacturing arrangements for Vasovist for commercial use, including the transfer of manufacturing to Bayer Schering Pharma AG, Germany. Covidien currently manufactures imaging agents for other technologies that will compete with Vasovist. In the event that Covidien fails to fulfill its manufacturing responsibilities satisfactorily, Bayer Schering Pharma AG, Germany has the right to purchase Vasovist from a third-party or to manufacture the compound itself. However, either course of action could materially delay the manufacture and development of Vasovist. Bayer Schering Pharma AG, Germany may not be able to find an alternative manufacturer. In addition, Bayer Schering Pharma AG, Germany may not be able to manufacture Vasovist itself in a timely manner or in sufficient quantities. If we experience a delay in manufacturing of Vasovist or any of our product candidates, it could result in a delay in their clinical testing, approval or commercialization and have a material adverse effect on our business, financial condition and results of operations.

***If we are unable to attract and retain key management and other personnel, it would hurt our ability to compete.***

Our future business and operating results depend in significant part upon our ability to attract and retain qualified directors, senior management and key technical personnel. Michael G. Kauffman, M.D., Ph.D., Andrew C.G. Uprichard, M.D. and Kim Cobleigh Drapkin, CPA, our Chief Executive Officer, President and Chief Financial Officer, respectively, are expected to play key roles moving forward. There can be no

assurance that we will be able to retain Dr. Kauffman, Dr. Uprichard, Ms. Drapkin or any of our other key management and scientific personnel. The loss of any of our key management and other personnel, or their failure to perform their current positions could have a material adverse effect on our business, financial condition and results of operations, and our ability to achieve our business objectives or to operate or compete in our industry may be seriously impaired. Competition for personnel is intense and we may not be successful in attracting or retaining such personnel. If we were to lose these employees to our competition, we could spend a significant amount of time and resources to replace them, which would impair our research and development or commercialization efforts.

***Our research and development efforts may not result in product candidates appropriate for testing in human clinical trials.***

We have historically spent significant resources on research and development and preclinical studies of product candidates. However, these efforts may not result in the development of product candidates appropriate for testing in human clinical trials. For example, our research may result in product candidates that are not expected to be effective in treating diseases or may reveal safety concerns with respect to product candidates. We may postpone or terminate research and development of a product candidate or a program at any time for any reason such as the safety or effectiveness of the potential product, allocation of resources or unavailability of qualified research and development personnel. The failure to generate high-quality research and development candidates would negatively impact our ability to advance product candidates into human clinical testing and ultimately, negatively impact our ability to market and sell products.

***If we fail to get adequate levels of reimbursement from third-party payors for our product candidates after they are approved in the United States and abroad, we may have difficulty commercializing our product candidates.***

We believe that reimbursement in the future will be subject to increased restrictions, both in the United States and in foreign markets. We believe that the overall escalating cost of medical products and services has led to, and will continue to lead to, increased pressures on the health care industry, both foreign and domestic, to reduce the cost of products and services, including products offered by us. These third-party payors are increasingly attempting to contain healthcare costs by demanding price discounts or rebates and limiting both coverage on which drugs they will pay for and the amounts that they will pay for new products. As a result, they may not cover or provide adequate payment for our products. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payors' satisfaction. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. There can be no assurance, in either the United States or foreign markets, that third-party reimbursement will be available or adequate, that current reimbursement amounts will not be decreased in the future or that future legislation, regulation, or reimbursement policies of third-party payors will not otherwise adversely affect the demand for our product candidates or our ability to sell our product candidates on a profitable basis. The unavailability or inadequacy of third-party payor coverage or reimbursement could have a material adverse effect on our business, financial condition and results of operations.

Failure by physicians, hospitals and other users of our product candidate to obtain sufficient reimbursement from third-party payors for the procedures in which our product candidate would be used or adverse changes in governmental and private third-party payors' policies toward reimbursement for such procedures may have a material adverse effect on our ability to market our product candidate and, consequently, it could have an adverse effect on our business, financial condition and results of operations. If we obtain the necessary foreign regulatory approvals, market acceptance of our product candidates in international markets would be dependent, in part, upon the availability of reimbursement within prevailing healthcare payment systems. Reimbursement and healthcare payment systems in international markets vary significantly by country, and include both government sponsored health care and private insurance. We and our strategic partners intend to seek international reimbursement approvals, although we cannot assure you that any such approvals will be obtained in a timely manner, if at all, and failure to receive international

reimbursement approvals could have an adverse effect on market acceptance of our product candidate in the international markets in which such approvals are sought.

We could be adversely affected by changes in reimbursement policies of governmental or private healthcare payors, particularly to the extent any such changes affect reimbursement for procedures in which our product candidates would be used. U.S. and foreign governments continue to propose and pass legislation designed to reduce the cost of healthcare. For example, in some foreign markets, the government controls the pricing of prescription pharmaceuticals. In the United States, we expect that there will continue to be federal and state proposals to implement similar governmental controls. In addition, recent changes in the Medicare program and increasing emphasis on managed care in the United States will continue to put pressure on pharmaceutical product pricing. Cost control initiatives could decrease the price that we would receive for any products in the future, which would limit our revenue and profitability. Accordingly, legislation and regulations affecting the pricing of pharmaceuticals might change before our product candidates are approved for marketing. Adoption of such legislation could further limit reimbursement for pharmaceuticals.

***We deal with hazardous materials and must comply with environmental laws and regulations, which can be expensive and restrict how we do business.***

The nature of our research and development processes requires the use of hazardous substances and testing on certain laboratory animals. Accordingly, we are subject to extensive federal, state and local laws, rules, regulations and policies governing the use, generation, manufacture, storage, air emission, effluent discharge, handling and disposal of certain materials and wastes as well as the use of and care for laboratory animals. Although we are not currently, nor have we been, the subject of any investigations by a regulatory authority, we cannot assure you that we will not become the subject of any such investigation. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials.

In the event of an accident, state or federal authorities may curtail our use of these materials and interrupt our business operations. In addition, we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. Due to the small amount of hazardous materials that we generate, we have determined that the cost to secure insurance coverage for environmental liability and toxic tort claims far exceeds the benefits. Accordingly, we do not maintain any insurance to cover pollution conditions or other extraordinary or unanticipated events relating to our use and disposal of hazardous materials. Additionally, an accident could damage, or force us to shut down, our operations. In addition, if we develop a manufacturing capacity, we may incur substantial costs to comply with environmental regulations and would be subject to the risk of accidental contamination or injury from the use of hazardous materials in our manufacturing process. Furthermore, current laws could change and new laws could be passed that may force us to change our policies and procedures, an event which could impose significant costs on us.

***Product liability claims could increase our costs and adversely affect our results of operations.***

The clinical testing of our products and the manufacturing and marketing of any approved products may expose us to product liability claims and we may experience material product liability losses in the future. We currently have limited product liability insurance for the use of our approved products and product candidates in clinical research, which is capped at \$10.0 million, but our coverage may not continue to be available on terms acceptable to us or adequate for liabilities we actually incur. We do not have product liability insurance coverage for the commercial sale of our product candidates, but intend to obtain such coverage when and if we commercialize our product candidates. However, we may not be able to obtain adequate additional product liability insurance coverage on acceptable terms, if at all. A successful claim brought against us in excess of available insurance coverage, or any claim or product recall that results in significant adverse publicity against us, may have a material adverse effect on our business and results of operations.

***Political and military instability and other factors may adversely affect our operations in Israel.***

We have significant operations in Israel and regional instability, military conditions, terrorist attacks, security concerns and other factors in Israel may directly affect these operations. Our employees in Israel are primarily computational chemists and are responsible for the computational chemistry for all of our therapeutic discovery stage programs. Accordingly, any disruption in our Israeli operations could adversely affect our ability to advance our therapeutic discovery stage programs into clinical trials. Since the establishment of the State of Israel in 1948, a number of armed conflicts have taken place between Israel and its Arab neighbors. A state of hostility, varying in degree and intensity, has led to security and economic problems for Israel, and in particular since 2000, there has been an increased level of violence between Israel and the Palestinians. Any armed conflicts or political instability in the region could harm our operations in Israel. In addition, many of our employees in Israel are obligated to perform annual military reserve duty, and, in the event of a war, military or other conflict, our employees could be required to serve in the military for extended periods of time. Our operations could be disrupted by the absence for a significant period of time of one or more of our key employees or a significant number of our other employees due to military service. Furthermore, several countries restrict business with Israel and Israeli companies, and these restrictive laws and policies could harm our business.

**RISKS RELATED TO OUR INTELLECTUAL PROPERTY**

***We depend on patents and other proprietary rights, and if they fail to protect our business, we may not be able to compete effectively.***

The protection of our proprietary technologies is material to our business prospects. We pursue patents for our product candidates in the United States and in other countries where we believe that significant market opportunities exist. We own or license patents and patent applications on aspects of our core technology as well as many specific applications of this technology. As of February 28, 2008, our patent portfolio included a total of 16 issued U.S. patents, 117 issued foreign patents, and 277 pending patent applications in the U.S. and other countries with claims covering the composition of matter and methods of use for all of our preclinical and clinical-stage product candidates. We also exclusively license technology embodied in patent applications from Ramot at Tel Aviv University Ltd., the technology transfer company of Tel Aviv University. Physiome Sciences, Inc., a predecessor of Predix, received U.S. Patent 5,947,899, which covers a computational system and method for modeling the heart. This patent expires in 2016. Even though we hold numerous patents and have made numerous patent applications, because the patent positions of pharmaceutical and biopharmaceutical firms, including our patent positions, generally include complex legal and factual questions, our patent positions remain uncertain. For example, because most patent applications are maintained in secrecy for a period after filing, we cannot be certain that the named applicants or inventors of the subject matter covered by our patent applications or patents, whether directly owned or licensed to us, were the first to invent or the first to file patent applications for such inventions. Third-parties may oppose, challenge, infringe upon, circumvent or seek to invalidate existing or future patents owned by or licensed to us. A court or other agency with jurisdiction may find our patents invalid, not infringed or unenforceable and we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future. Even if we have valid patents, these patents still may not provide sufficient protection against competing products or processes. If we are unable to successfully protect our proprietary methods and technologies, or if our patent applications do not result in issued patents, we may not be able to prevent other companies from practicing our technology and, as a result, our competitive position may be harmed.

***We depend on exclusively licensed technology from Ramot at Tel Aviv University Ltd. and Massachusetts General Hospital and, if we lose either of these licenses, it is unlikely we could obtain such technology elsewhere, which would have a material adverse effect on our business.***

Our proprietary drug discovery technology and approach is in part embodied in technology that we license from Ramot at Tel Aviv University Ltd., the technology transfer company of Tel Aviv University. All of our current clinical-stage therapeutic drug candidates, PRX-00023, PRX-03140, PRX-08066 and PRX-

07034, were, at least in part, identified, characterized or developed using the licensed technology. We are required to make various payments to Ramot, as and when rights to any such drug candidates are ever sublicensed or any such drug candidates are commercialized. Because we have an ongoing obligation to pay annual minimum royalties to Ramot and the license expires upon the expiration of such obligation, the license may not expire. The license may, however, be terminated upon a breach by us or our bankruptcy. In addition, under the terms of a license agreement that we have with MGH, we are the exclusive licensee to certain imaging technology, which relates to royalties we receive and to Vasovist. The license agreement imposes various commercialization, sublicensing, royalty and other obligations on us. The license agreement expires on a country-by-country basis when the patents covered by the license agreement expire. The majority of these patents expired in November 2006. One of these patents has been extended through Supplementary Protection Certificates for Primovist through May 2011 in certain European countries. The license agreement does not contain a renewal provision. If we fail to comply with our obligations under either of these license agreements, the respective license could convert from exclusive to nonexclusive, or terminate entirely. It is unlikely that we would be able to obtain the technology licensed under either of these agreements elsewhere. Any such event would also mean that, with respect to our MGH license, we would not receive royalties from Bayer Schering Pharma AG, Germany for Primovist and that we or Bayer Schering Pharma AG, Germany could not sell Vasovist and, with respect to our Ramot license, that we would not be able to sublicense or commercialize any of our current clinical-stage therapeutic drug candidate, either of which would have a material adverse effect on our business and our financial condition and results of operations.

***We may need to initiate lawsuits to protect or enforce our patents and other intellectual property rights, which could result in our incurrence of substantial costs and which could result in the forfeiture of these rights.***

We may need to bring costly and time-consuming litigation against third-parties in order to enforce our issued or licensed patents, protect our trade secrets and know how, or to determine the enforceability, scope and validity of proprietary rights of others. In addition to being costly and time-consuming, such lawsuits could divert management's attention from other business concerns. These lawsuits could also result in the invalidation or a limitation in the scope of our patents or forfeiture of the rights associated with our patents or pending patent applications. We may not prevail and a court may find damages or award other remedies in favor of an opposing party in any such lawsuits. During the course of these suits, there may be public announcements of the results of hearings, motions and other interim proceedings or developments in the litigation. Securities analysts or investors may perceive these announcements to be negative, which could cause the market price of our stock to decline. In addition, the cost of such litigation could have a material adverse effect on our business and financial condition.

***Other rights and measures that we rely upon to protect our intellectual property may not be adequate to protect our products and services and could reduce our ability to compete in the market.***

In addition to patents, we rely on a combination of trade secrets, copyright and trademark laws, non-disclosure agreements and other contractual provisions and technical measures to protect our intellectual property rights. While we require employees, collaborators, consultants and other third-parties to enter into confidentiality and/or non-disclosure agreements, where appropriate, any of the following could still occur:

- the agreements may be breached;
- we may have inadequate remedies for any breach;
- proprietary information could be disclosed to our competitors; or
- others may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose such technologies.

If, as a result of the foregoing or otherwise, our intellectual property is disclosed or misappropriated, it would harm our ability to protect our rights and our competitive position. Moreover, several of our management and scientific personnel were formerly associated with other pharmaceutical and biotechnology

companies and academic institutions. In some cases, these individuals are conducting research in similar areas with which they were involved prior to joining us. As a result, we, as well as these individuals, could be subject to claims of violation of trade secrets and similar claims.

***Our success will depend partly on our ability to operate without infringing the intellectual property rights of others, and if we are unable to do so, we may not be able to sell our products.***

Our commercial success will depend, to a significant degree, on our ability to operate without infringing upon the patents of others in the United States and abroad. There may be pending or issued patents held by parties not affiliated with us relating to technologies we use in the development or use of certain of our contrast agents. If any judicial or administrative proceeding upholds these or any third-party patents as valid and enforceable, we could be prevented from practicing the subject matter claimed in such patents, or would be required to obtain licenses from the owners of each such patent, or to redesign our product candidates or processes to avoid infringement. For example, in November 2003, we entered into an intellectual property agreement with Dr. Martin R. Prince relating to "dynamic" magnetic resonance angiography. Under the terms of the intellectual property agreement, Dr. Prince granted us certain discharges, licenses and releases in connection with the historic and future use of Vasovist by us and agreed not to sue us for intellectual property infringement related to the use of Vasovist. We were required to pay an upfront fee of \$850,000, royalties on sales of Vasovist and approximately 88,000 shares of our common stock with a value of approximately \$2.3 million based on the closing price of our common stock on the date of the agreement. In addition, we agreed to supply Dr. Prince with approximately \$140,000 worth of Vasovist annually throughout the patent life of Vasovist. We cannot assure you that we will be able to enter into additional licenses if required in the future. If we are unable to obtain a required license on acceptable terms, or are unable to design around these or any third-party patents, we may be unable to sell our products, which would have a material adverse effect on our business.

***If MRI manufacturers are not able to enhance their hardware and software sufficiently, we will not be able to complete development of our contrast agent for the evaluation of cardiac indications.***

Although MRI hardware and software is sufficient for the evaluation of non-coronary vascular disease, which is our initial target indication, we believe that the technology is not as advanced for cardiac applications. Our initial NDA filing for Vasovist is related to non-coronary vascular disease. Based on feasibility studies we completed in 2001, however, the imaging technology available for cardiac applications, including coronary angiography and cardiac perfusion imaging, was not developed to the point where there was clear visualization of the cardiac region due to the effects of motion from breathing and from the beating of the heart. In 2004, we initiated Phase 2 feasibility trials of Vasovist for cardiac indications using available software and hardware that can be adapted for coronary and cardiac perfusion data acquisition, and preliminary review of the data indicates that we have not resolved the technical issues related to this use of Vasovist. We have collaborated with a number of leading academic institutions and with GE Healthcare, Siemens Medical Systems and Philips Medical Systems to help optimize cardiac imaging with Vasovist. We do not know when, or if, these techniques will enable Vasovist to provide clinically relevant images in cardiac indications. If MRI device manufacturers are not able to enhance their scanners to perform clinically useful cardiac imaging, we will not be able to complete our development activities of Vasovist for that application, thereby reducing the potential market for a product in this area.

## **RISKS RELATED TO OUR SECURITIES**

***Our stock price is volatile, which could subject us to securities class action litigation.***

The market prices of the capital stock of medical technology companies have historically been very volatile and the market price of the shares of our common stock fluctuates. The market price of our common stock is affected by numerous factors, including:

- actual or anticipated fluctuations in our operating results;
- announcements of technological innovation or new commercial products by us or our competitors;

- new collaborations entered into by us or our competitors;
- developments with respect to proprietary rights, including patent and litigation matters;
- results of preclinical studies and clinical trials;
- the timing of our achievement of regulatory milestones;
- conditions and trends in the pharmaceutical and other technology industries;
- adoption of new accounting standards affecting such industries;
- changes in financial estimates by securities analysts;
- perceptions of the value of corporate transactions; and
- degree of trading liquidity in our common stock and general market conditions.

From the closing of our merger with Predix and our 1 for 1.5 share reverse stock split on August 16, 2006 to March 14, 2008, the closing price of our common stock ranged from \$2.67 to \$7.58 per share. The last reported closing price for our common stock on March 14, 2008 was \$2.85. Significant declines in the price of our common stock could impede our ability to obtain additional capital, attract and retain qualified employees and reduce the liquidity of our common stock.

In addition, the stock market has from time to time experienced significant price and volume fluctuations that have particularly affected the market prices for the common stock of similarly staged companies. These broad market fluctuations may adversely affect the market price of our common stock. In the past, following periods of volatility in the market price of a particular company's securities, shareholders have often brought class action securities litigation against that company. Such litigation could result in substantial costs and a diversion of management's attention and resources. For example, in January 2005, a securities class action was filed in U.S. District Court for the District of Massachusetts against us and certain of our officers on behalf of persons who purchased our common stock between July 10, 2003 and January 14, 2005. The complaint alleged that we and the other defendants violated the Securities Exchange Act of 1934, as amended, by issuing a series of materially false and misleading statements to the market throughout the class period, which statements had the effect of artificially inflating the market price of our securities. In January 2006, the U.S. District Court for the District of Massachusetts granted our Motion to Dismiss for Failure to Prosecute the shareholder class action lawsuit against us. The dismissal was issued without prejudice after a hearing, which dismissal does not prevent another suit to be brought based on the same claims.

***Future sales of common stock by our existing stockholders and former security holders of Predix may cause the stock price of our common stock to fall.***

The market price of our common stock could decline as a result of sales by our existing stockholders and former Predix stockholders in the market, or the perception that these sales could occur. These sales might also make it more difficult for us to sell equity securities at an appropriate time and price.

***Certain anti-takeover clauses in our charter and by-laws and in Delaware law may make an acquisition of us more difficult.***

Our restated certificate of incorporation authorizes our board of directors to issue, without stockholder approval, up to 1,000,000 shares of preferred stock with voting, conversion and other rights and preferences that could adversely affect the voting power or other rights of the holders of our common stock. The issuance of preferred stock or of rights to purchase preferred stock could be used to discourage an unsolicited acquisition proposal. In addition, the possible issuance of preferred stock could discourage a proxy contest, make more difficult the acquisition of a substantial block of our common stock or limit the price that investors might be willing to pay for shares of our common stock. Our restated certificate of incorporation provides for staggered terms for the members of our board of directors. A staggered board of directors and certain provisions of our by-laws and of the state of Delaware law applicable to us could delay or make more difficult a merger, tender offer or proxy contest involving us. We are subject to Section 203 of the General Corporation

Law of the State of Delaware, which, subject to certain exceptions, restricts certain transactions and business combinations between a corporation and a stockholder owning 15% or more of the corporation's outstanding voting stock for a period of three years from the date the stockholder becomes an interested stockholder. These provisions may have the effect of delaying or preventing a change in control of us without action by the stockholders and, therefore, could adversely affect the price of our stock.

#### **ITEM 1B. *UNRESOLVED STAFF COMMENTS***

None.

#### **ITEM 2. *PROPERTIES***

We lease a total of 57,300 square feet of space at our 4 Maguire Road, Lexington, Massachusetts location and 9,200 square feet of space at our 3 Hayetzira Street, Ramat Gan, Israel location. The lease at 4 Maguire Road expires October 2013 and the lease at 3 Hayetzira Street, Israel expires January 31, 2009. We believe that our current facilities are adequate to meet our needs until the expiration of the leases.

#### **ITEM 3. *LEGAL PROCEEDINGS***

From time to time we are a party to various legal proceedings arising in the ordinary course of our business. The outcome of litigation cannot be predicted with certainty and some lawsuits, claims or proceedings may be disposed of unfavorably to us. Intellectual property disputes often have a risk of injunctive relief which, if imposed against us, could materially and adversely affect our financial condition, or results of operations. From time to time, third-parties have asserted and may in the future assert intellectual property rights to technologies that are important to our business and have demanded and may in the future demand that we license their technology.

On December 8, 2006, we created a special board committee of independent directors to conduct a review of our historical stock option practices. The special committee completed its investigation and concluded that certain employees, including certain members of our former senior management, prior to the change in our senior management in connection with the merger with Predix in August 2006, had retrospectively selected dates for the grant of certain stock options and re-priced, as defined by financial accounting standards, certain options during the period from 1997 through 2005. As a result, in connection with the filing of our 2006 Form 10-K, we restated our financial statements to record additional non-cash stock-based compensation expense and related payroll tax effects, with regard to these past stock option grants. The SEC is conducting an informal inquiry into our stock option grants and practices and related accounting. Our past stock option practices and the restatement of our prior financial statements expose us to greater risks associated with litigation, regulatory, or other proceedings, as a result of which we could be required to pay significant fines or penalties.

#### **ITEM 4. *SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS***

No matters were submitted to a vote of our security holders, whether through the solicitation of proxies or otherwise, during our 2007 fourth fiscal quarter.

## PART II

### ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our Common Stock is listed on The NASDAQ Global Market under the symbol "EPIX." All prices reflect our 1 for 1.5 share reverse stock split effected on August 16, 2006 in connection with the closing of our merger with Predix.

The following table sets forth, for the periods indicated, the range of the high and low sales prices for our Common Stock as reported on The NASDAQ Global Market:

	<u>High</u>	<u>Low</u>
<b>2006</b>		
First Quarter .....	\$7.76	\$5.00
Second Quarter .....	7.25	4.05
Third Quarter .....	8.35	4.05
Fourth Quarter .....	8.75	3.50
<b>2007</b>		
First Quarter .....	7.20	6.08
Second Quarter .....	7.28	5.08
Third Quarter .....	5.90	3.67
Fourth Quarter .....	5.40	2.89

The above quotations reflect inter-dealer prices without retail mark-up, markdown or commission and may not necessarily represent actual transactions.

On March 14, 2008, the last reported price for the common stock was \$2.85 per share. As of March 14, 2008, there were 235 holders of record of the 41,355,575 outstanding shares of Common Stock. To date, we have neither declared nor paid any cash dividends on shares of our Common Stock and do not anticipate doing so for the foreseeable future.

During the quarter ended December 31, 2007, there were no repurchases made by us or on our behalf, or by any "affiliated purchaser," of shares of our common stock.

### EQUITY COMPENSATION PLAN INFORMATION

We maintain the following three equity compensation plans under which our equity securities are authorized for issuance to our employees, directors and consultants: Amended and Restated 1992 Incentive Plan; Amended and Restated 1996 Director Stock Option Plan; and Amended and Restated 2003 Stock Incentive Plan. The following table represents information about these plans as of December 31, 2007:

<u>Plan Category</u>	<u>(A)</u>	<u>(B)</u>	<u>(C)</u>
	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (A))
Equity compensation plans approved by security holders . . .	2,517,105	\$9.36	666,084
Equity compensation plans not approved by security holders(1) . . . . .	<u>1,330,281</u>	\$2.09	<u>922,113</u>
Total . . . . .	<u>3,847,386</u>	\$6.85	<u>1,588,197</u>

(1) Represents the Predix Pharmaceuticals Holdings, Inc. Amended and Restated 2003 Stock Incentive Plan assumed in our 2006 merger with Predix.

## ITEM 6. *SELECTED FINANCIAL DATA*

The following table sets forth consolidated financial data for each of the five years in the period ending December 31, 2007. In thousands, except per share data.

	Year Ended December 31,				
	2007	2006(1)	2005	2004	2003
<b>Statement of Operations Data:</b>					
Revenues . . . . .	\$ 14,960	\$ 6,041	\$ 7,190	\$ 12,259	\$ 13,525
Operating loss . . . . .	(63,564)	(157,668)	(21,760)	(22,351)	(26,008)
Net loss . . . . .	(62,789)	(157,393)	(21,269)	(22,621)	(25,720)
Weighted average common shares outstanding:					
Basic and diluted . . . . .	33,936	20,789	15,505	15,259	12,704
Net loss per share, basic and diluted . . . . .	\$ (1.85)	\$ (7.57)	\$ (1.37)	\$ (1.48)	\$ (2.02)

	December 31,				
	2007	2006	2005	2004	2003
<b>Balance Sheet Data:</b>					
Cash, cash equivalents and marketable securities . . . . .	\$ 61,077	\$109,543	\$124,728	\$164,440	\$79,958
Total assets . . . . .	78,075	125,027	130,716	171,287	81,875
Convertible debt . . . . .	100,000	100,000	100,000	100,000	—
Total long-term liabilities . . . . .	120,846	120,066	100,756	101,210	4,331

(1) The company merged with Predix on August 16, 2006. 2006 includes a charge of \$123.5 million for acquired in-process research and development related to the merger.

The information below should be read in conjunction with the consolidated financial statements (and notes thereon) and "Management's Discussion and Analysis of Financial Condition and Results of Operations," included in Item 7.

## ITEM 7. *MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS*

The information contained in this section has been derived from our consolidated financial statements and should be read together with our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

### Overview

We are a biopharmaceutical company focused on discovering, developing and commercializing novel pharmaceutical products through the use of proprietary technologies to better diagnose, treat and manage patients. We have four internally discovered therapeutic product candidates in clinical trials targeting conditions such as depression, Alzheimer's disease, cardiovascular disease and cognitive impairment. Our blood-pool imaging agent, Vasovist, is approved for marketing in over 30 countries outside of the United States. We also have collaborations with SmithKline Beecham Corporation (GlaxoSmithKline), Amgen Inc., Cystic Fibrosis Foundation Therapeutics, Incorporated, and Bayer Schering Pharma AG, Germany. Our business strategy is to develop our internally discovered, novel pharmaceutical products through the point of proof of clinical concept, typically completion of Phase 2 clinical trials and then to seek pharmaceutical partnerships for the continued development, regulatory approvals and world-wide commercialization of the product

candidates. In certain disease areas, such as pulmonary hypertension, where we believe we can efficiently obtain regulatory approval and effectively market the product through a specialty sales force, we may seek to retain commercialization rights in the United States.

The focus of our therapeutic drug discovery and development efforts is on the two classes of drug targets known as G-protein Coupled Receptors, or GPCRs, and ion channels. GPCRs and ion channels are classes of proteins embedded in the surface membrane of all cells and are responsible for mediating much of the biological signaling at the cellular level. We believe that our proprietary drug discovery technology and approach addresses many of the inefficiencies associated with traditional GPCR and ion channel-targeted drug discovery. By integrating computer-based, or in silico, technology with in-house medicinal chemistry, we believe that we can rapidly identify and optimize highly selective drug candidates. We focus on GPCR and ion channel drug targets whose role in disease has already been demonstrated in clinical trials or in preclinical studies. In each of our four clinical-stage therapeutic programs, we used our drug discovery technology and approach to optimize a lead compound into a clinical drug candidate in less than ten months, synthesizing fewer than 80 compounds per program. We moved each of these drug candidates into clinical trials in less than 18 months from lead identification. We believe our drug discovery technology and approach enables us to efficiently and cost-effectively discover and develop GPCR and ion channel-targeted drugs.

On August 16, 2006, we completed our acquisition of Predix Pharmaceuticals Holdings, Inc. pursuant to the terms of that certain Agreement and Plan of Merger, dated as of April 3, 2006 as amended on July 10, 2006, by and among us, EPIX Delaware, Inc., our wholly-owned subsidiary, and Predix, as amended. Pursuant to the merger agreement, Predix merged with and into EPIX Delaware, Inc. and became a wholly-owned subsidiary of us. The merger with Predix was primarily a stock transaction valued at approximately \$125.0 million, including the assumption of net debt at closing. As part of the merger, we also assumed all outstanding options and warrants to purchase capital stock of Predix. The purchase price included a \$35.0 million milestone payment to the holders of Predix stock, options and warrants payable in cash, stock or a combination of both. Pursuant to the terms of the merger agreement, \$20.0 million of the milestone was paid in cash on October 29, 2006. The remaining \$15.0 million of the milestone payment, including accrued interest, was paid on October 29, 2007 through the issuance of 3,167,000 common shares and the payment of \$5.8 million in cash.

### **Critical Accounting Policies And Estimates**

The discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect our reported assets and liabilities, revenues and expenses, and other financial information. Actual results may differ significantly from the estimates under different assumptions and conditions.

Our significant accounting policies are more fully described in Note 2 of our Consolidated Financial Statements for the year ended December 31, 2007. Not all significant accounting policies require management to make difficult, subjective or complex judgments or estimates. We believe that our accounting policies related to revenue recognition, research and development and employee stock compensation, as described below, require "critical accounting estimates and judgments."

#### ***Revenue Recognition***

We recognize revenue relating to collaborations in accordance with the Securities and Exchange Commission's, or SEC's, Staff Accounting Bulletin (SAB) No. 104, "*Revenue Recognition*," or SAB 104. Revenue under collaborations may include the receipt of non-refundable license fees, milestone payments, and research and development payments and royalties.

We recognize nonrefundable upfront license fees and guaranteed, time-based payments that require continuing involvement in the form of research and development as license fee revenue:

- ratably over the development period; or
- based upon the level of research services performed during the period of the research contract.

When the period of deferral cannot be specifically identified from the contract, we estimate the period based upon other critical factors contained within the contract. We continually review such estimates which could result in a change in the deferral period and might impact the timing and amount of revenue recognized.

Milestone payments which represent a significant performance risk are recognized as product development revenue when the performance obligations, as defined in the contract, are achieved. Performance obligations typically consist of significant milestones in the development life cycle of the related technology, such as the filing of investigational new drug applications, initiation of clinical trials, filing for approval with regulatory agencies and approvals by regulatory agencies. Milestone payments which are received at the time of initiation of a collaboration agreement or do not represent a significant performance risk are recognized ratably over the development period.

Reimbursements of research and development costs are recognized as product development revenue as the related costs are incurred.

Royalties are recognized as revenue when earned, reasonably estimable and collection is probable, which is typically upon receipt of royalty reports from the licensee or cash.

### ***Product development revenue***

We recognize as revenue from Bayer Schering Pharma AG, Germany costs incurred by us in excess of our obligation under the agreement to expend 50% of the costs to develop Vasovist. This revenue is recognized in the same period in which the costs are incurred. With respect to payments due to Bayer Schering Pharma AG, Germany, if any, in connection with the Vasovist development program, we recognize such amounts as a reduction in revenue at the time Bayer Schering Pharma AG, Germany performs the research and development activities for which we are obligated to pay Bayer Schering Pharma AG, Germany.

On a quarterly basis, we calculate the revenue or reduction in revenue, as the case may be, with respect to the collaboration with Bayer Schering Pharma AG, Germany for Vasovist as follows:

- We calculate our development costs directly related to Vasovist.
- We obtain cost reports from Bayer Schering Pharma AG, Germany for costs incurred by Bayer Schering Pharma AG, Germany related to the development of Vasovist during the same period.
- We multiply our and Bayer Schering Pharma AG, Germany's development costs by approximately 50% based on the contractual allocation of work contemplated under the agreement.
- We then record the net difference as development revenue if the balance results in a payment to us and negative revenue if the balance results in a payment to Bayer Schering Pharma AG, Germany.

The result of this calculation is that we record revenue only for amounts we are owed by Bayer Schering Pharma AG, Germany in excess of 50% of development expenses of the project in the particular period. We record a reduction to revenue for any amounts owed to Bayer Schering Pharma AG, Germany in the particular period.

We also recognize as revenue from GlaxoSmithKline and Cystic Fibrosis Foundation Therapeutics, Incorporated certain third-party costs incurred by us and internal development efforts in the performance of research activities under the related contracts. Internal development efforts are billed at standard rates under the contracts. This revenue is recognized in the same period in which the costs are incurred.

### ***Royalty revenue***

We are entitled to receive a royalty on worldwide sales of Primovist and on sales of Vasovist outside of the United States by Bayer Schering Pharma AG, Germany. Royalty revenue is recognized based on actual revenues or gross profits as reported by Bayer Schering Pharma AG, Germany to us in the period in which royalty reports are received.

### ***License fee revenue***

We record license fee revenue in accordance with SAB 104, "*Revenue Recognition*." Pursuant to SAB 104, we recognize revenue from non-refundable license fees and milestone payments, not specifically tied to a separate earnings process, ratably over the period during which we have a substantial continuing obligation to perform services under the contract. Certain contracts require judgment to determine the period of continuing involvement by us and these estimates are subject to change based upon changes in facts and circumstances. When milestone payments are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligations associated with the payment are completed.

### ***Research and Development***

We account for research and development costs in accordance with Statement of Financial Accounting Standards (SFAS) No. 2, "*Accounting for Research and Development Cost*," which requires that expenditures be expensed to operations as incurred.

Research and development expenses primarily include employee salaries and related costs, third-party service costs, the cost of preclinical and clinical trials, supplies, consulting expenses, facility costs and certain overhead costs.

In order to conduct research and development activities and compile regulatory submissions, we enter into contracts with vendors who render services over extended periods of time. Typically, we enter into three types of vendor contracts: time-based, patient-based or a combination thereof. Under a time-based contract, using critical factors contained within the contract, usually the stated duration of the contract and the timing of services provided, we record the contractual expense for each service provided under the contract ratably over the period during which we estimate the service will be performed. Under a patient-based contract, we first determine an appropriate per patient cost using critical factors contained within the contract, which include the estimated number of patients and the total dollar value of the contract. We then record expense based upon the total number of patients enrolled in the clinical study during the period. On a quarterly basis, we review the assumptions for each contract in order to reflect our most current estimate of the costs incurred under each contract. Adjustments are recorded in the period in which the revisions are estimable. These adjustments could have a material effect on our results of operations.

### ***Employee Stock Compensation***

We have adopted the provisions of SFAS No. 123(R), "*Share-Based Payment — An Amendment of FASB Statements No. 123 and 95*," or SFAS 123(R), beginning January 1, 2006, using the modified prospective transition method. Under the modified prospective transition method, financial statements for periods prior to the adoption date are not adjusted for the change in accounting. However, compensation expense is recognized, based on the requirements of SFAS 123(R), for (a) all share-based payments granted after the effective date and (b) all awards granted to employees prior to the effective date that remain unvested on the effective date.

Determining the appropriate fair value model and calculating the fair value of share-based awards requires us to make various judgments, including estimating the expected life of the share-based award, the expected stock price volatility over the expected life of the share-based award and forfeiture rates. In order to determine the fair value of share-based awards on the date of grant, we use the Black-Scholes option-pricing model. Inherent in this model are assumptions related to stock price volatility, option life, risk-free interest rate and dividend yield. The risk-free interest rate is a less subjective assumption as it is based on treasury instruments whose term is consistent with the expected life of options. We use a dividend yield of zero as we have never paid cash dividends and have no intention to pay cash dividends in the foreseeable future. The stock price volatility and option life assumptions require a greater level of judgment. Estimating forfeitures also requires significant judgment. Our stock-price volatility assumption is based on trends in both our current and historical volatilities of our stock and those of comparable companies. We use the "simplified" method, as prescribed by the SEC's SAB No. 107, to calculate the expected term of options. We estimate forfeitures based on our historical experience of cancellations of share-based compensation prior to vesting. We believe that our

estimates are based on outcomes that are reasonably likely to occur. To the extent actual forfeitures differ from our estimates, we will record an adjustment in the period the estimates are revised.

## Results of Operations

### *Research and Development Overview*

Research and development expense consists primarily of:

- salaries, benefits and related expenses for personnel engaged in research and development activities;
- fees paid to contract research organizations to manage and monitor clinical trials;
- fees paid to research organizations in conjunction with preclinical studies;
- fees paid to access chemical and intellectual property databases;
- costs of materials used in research and development and clinical studies;
- academic testing and consulting, license and sponsored research fees paid to third-parties; and
- costs of facilities and equipment, including depreciation, used in research and development activities.

We expense both internal and external research and development costs as incurred. We expect that a large percentage of our research and development expenses in the future will be incurred in support of our current and future preclinical and clinical development programs. These expenditures are subject to numerous uncertainties in timing and cost to completion. We test drug candidates in preclinical studies for safety, toxicology and efficacy. We then conduct early-stage clinical trials for each drug candidate. As we obtain results from trials, we may elect to discontinue or delay clinical trials for certain drug candidates in order to focus our resources on more promising drug candidates.

We currently have one imaging product, Vasovist, which is currently approved for marketing in more than 30 countries outside of the United States. In January 2008, based on written confirmation from the U.S. Food and Drug Administration, or FDA, regarding our protocol design and statistical analysis plan, we initiated a re-read of the images obtained in prior Phase 3 studies. As a result, future costs expected to be incurred for Vasovist are currently limited to the costs of performing the re-read of the Phase 3 clinical trial images and the submission of the results to the FDA.

In connection with our acquisition of Predix in 2006, we incurred a nonrecurring charge of \$123.5 million for in-process research and development. The in-process research and development charge represents the fair value of purchased in-process technology of Predix for research projects that, as of the closing date of the merger, had not reached technological feasibility and have no alternative future use. The in-process research and development primarily represents the estimated fair value of the following drug candidates: PRX-00023 (\$70.9 million) that, as of the date of the merger, was in a Phase 3 clinical trial for the treatment of generalized anxiety disorder; PRX-03140 (\$23.5 million) that, as of the date of the merger had completed Phase 1 clinical trials for the treatment of Alzheimer's disease; PRX-08066 (\$20.2 million) that, as of the date of the merger, had entered a Phase 2 clinical trial for the treatment of pulmonary hypertension in association with COPD; and PRX-07034 (\$8.9 million) that, as of the date of the merger, had entered a Phase 1 clinical trial for the treatment of obesity.

The following summarizes the applicable disease indication and the current clinical status of active therapeutic drug candidates:

<u>Drug Candidate</u>	<u>Disease Indication</u>	<u>Clinical Trial Status</u>
PRX-08066(1)	PH/COPD	Phase 2a
PRX-00023(2)	Depression	Phase 2b
PRX-03140(3)	Alzheimer's disease	Phase 2a
PRX-07034(4)	Cognitive impairment	Phase 1b

- 
- (1) We completed a Phase 2 trial of PRX-08066 in pulmonary hypertension associated with chronic obstructive pulmonary disease, or COPD, in August 2007. This randomized, double-blind, placebo-controlled Phase 2 trial enrolled 71 patients with PH associated with COPD. Patients were randomized to one of three arms; 200 mg of PRX-08066 once-daily; 400 mg of PRX-08066 once-daily; or placebo. The two-week double-blind phase of the study was followed by an open label extension in which 10 patients received 200 mg daily for six weeks. The primary endpoints of the trial were safety and tolerability of PRX-08066. Efficacy was measured by the effect of PRX-08066 compared to placebo on systolic pulmonary artery pressure, or SPAP, and included 62 evaluable patients who completed the double-blind portion of the study. In a population where decreases of 3 mmHg to 4 mmHg in a post-exercise SPAP are considered clinically significant, the results showed a statistically significant dose-response for the patients that demonstrated a decrease of 4 mmHg or more. In the 400 mg dose group, 45% of the patients had a reduction in post-exercise SPAP of 4 mmHg or more versus 14% on placebo ( $p=0.043$ ). An analysis of SPAP changes in all subjects revealed a dose trend with median reductions of 1.2 mmHg and 3.38 mmHg in the 200 mg and 400 mg dose groups, respectively, compared with no change on placebo. PRX-08066 was generally well-tolerated. There were no serious adverse events considered related to PRX-08066, and the majority of adverse events were mild or moderate in nature. One subject in the 200 mg dose group who then continued into the six-week open-label extension experienced a modest increase in liver enzyme levels at the end of the extension that was believed to be drug-related. These values returned to normal within two weeks and the subject remained asymptomatic.
  - (2) We have discontinued clinical development of PRX-00023 at a dose of 80 mg once daily in generalized anxiety disorder and are currently focusing our development efforts for this drug candidate on depression. In March 2007, we initiated a Phase 2b clinical trial to evaluate the efficacy of PRX-00023 in patients with a primary diagnosis of Major Depressive Disorder (MDD) who also have concurrent anxiety. The randomized, double-blind, placebo-controlled trial completed enrollment in October 2007, enrolling 362 adult patients with MDD, and is designed to evaluate the effect of treatment with up to 120 mg of PRX-00023 twice-daily for eight weeks as determined by change from baseline in the Montgomery Asberg Depression Rating Scale (MADRS) compared with placebo. All patients randomized to the drug treatment began with 40 mg PRX-00023 twice daily, and would increase the dose, if tolerated, to a maximum of 120 mg twice daily within the first week. Changes in the Hamilton Anxiety Score (HAM-A), Clinical Global Impressions Improvement Scale (CGI-I) and Clinical Global Severity of Illness Scale (CGI-S) were also measured. Results of the study are expected to be reported in March 2008.
  - (3) We completed a Phase 2 trial of PRX-03140 alone and in combination with an approved drug for Alzheimer's disease (the cholinesterase inhibitor Aricept (donepezil)) in patients with Alzheimer's disease in the fourth quarter of 2007. This randomized, double-blind, placebo-controlled, multiple ascending dose trial enrolled 80 patients with mild Alzheimer's disease. Patients were studied on PRX-03140 across three dose groups of 10 patients each: 50 mg once-daily, 150 mg once-daily and placebo, or in a placebo-controlled combination across five dose arms of 10 patients each: PRX-03140 at 5, 25, 50, 100 and 200 mg with Aricept 10 mg once-daily. The two primary endpoints of the trial were: (1) to assess the safety and tolerability of PRX-03140 in patients with Alzheimer's disease when dosed orally once-daily for 14 days alone and in combination with donepezil, and (2) to assess the effect of PRX-03140 on brain wave activity, as was performed in the Phase 1b clinical trial. Secondary endpoints of the trial included evaluating the pharmacokinetic effect of PRX-03140 on Aricept concentrations in patients with mild Alzheimer's disease and assessing the effects of repeat doses of PRX-03140 on a battery of standardized cognitive function tests, such as the Alzheimer's Disease Assessment Scale cognitive subscale (ADAS-cog).

Efficacy results show that patients receiving 150 mg of PRX-03140 orally once daily as monotherapy achieved a mean 3.6 point improvement on the ADAS-cog versus a 0.9 point worsening in patients on placebo. This result corresponds to a  $p$ -value of 0.021, which is statistically significant. Data for the patients on a 50 mg dose of PRX-03140 showed a 1.0 point improvement on the ADAS-cog. The monotherapy dose response (150 mg versus 50 mg versus placebo) was also statistically significant ( $p=0.026$ ). ADAS-cog changes in the combination arms of the trial were not statistically significant.

PRX-03140 appeared to be well tolerated in this trial, both alone and in combination with Aricept. No serious drug-related adverse events occurred during the trial.

- (4) In April 2007, we completed a Phase 1 multiple ascending dose clinical trial studying the safety, tolerability, pharmacokinetics, and pharmacodynamics of PRX-07034 administered once-daily for 28 days in a population of 33 otherwise healthy obese adults with body mass indices, or BMI, between 30 and 42 kg/m<sup>2</sup>. Normal BMI is less than 25 kg/m<sup>2</sup>. PRX-07034 demonstrated predictable pharmacokinetics with dose proportional increases in exposures, and a half-life supporting once-daily dosing. Signals suggestive of pharmacologic activity were observed for obesity with a greater proportion of subjects on drug experiencing weight loss during the one month period than subjects on placebo. Overall results on cognitive function as measured by the CogScreen test battery, showed a dose dependent trend for improvement. For the predetermined cognitive endpoint that combines speed and accuracy, there was a statistically significant improvement at the 600 mg dose once daily. Subsequently, an independent external analysis of the CogScreen test battery results confirmed a significant drug effect on cognition but was not able to confirm the dose-dependent trend. No dose limiting toxicity was identified, and no serious adverse events were reported.

In October 2007, we completed a randomized, double-blind, placebo-controlled Phase 1 trial of 21 obese, but otherwise healthy, adults. Findings from this study demonstrated that adults taking 600 mg of PRX-07034 twice-daily for 28 days had a weight reduction of an average of 0.45 kg (approximately 1 pound), while adults on placebo gained 1.37 kg (approximately 3 pounds) during the same period, which was statistically significant ( $p < 0.005$ ). Subjects in the study were not required to follow any pre-specified diet or exercise program. PRX-07034 was associated with a statistically significant ( $p=0.036$ ) reduction in serum leptin levels, a marker of fat stores in the body. Overall, only one of the subjects (approximately 10%) on placebo lost any weight during the trial, while 7 of the 11 subjects (approximately 64%) on PRX-07034 lost weight. PRX-07034 appeared well-tolerated and there were no serious adverse events reported. An increase in corrected QT interval, or QTc, was apparent at the dose tested, however, with a mean increase over the duration of the study of 10.7 milliseconds for the drug group versus a decrease of 1.7 milliseconds for the placebo group. The corrected QTc is a measurement of the QT interval, which is corrected for heart rate. Prolongations of the QTc are associated with an increased risk for potentially life-threatening heart rhythms and so this measurement is an important index to measure during the development of new drugs. In addition, of the population of 21 adults, one patient on drug discontinued due to a rash that resolved rapidly. There were no discontinuations on placebo. In the prior Phase 1 trial where doses up to 600 mg once daily were studied for 28 days, no clinically meaningful prolongations of the QTc were noted.

The 21-person trial, which was conducted in an outpatient setting (subjects spent three nights of the total 28-day trial as inpatients to accommodate measurements and physical examinations), included secondary endpoint measures to assess potential effects on body weight, hunger, satiety and exploratory endpoint measures of cognitive function. An analysis of cognitive data in this study showed no difference between drug and placebo at a dose of 600 mg twice daily. Accordingly, future studies in cognitive impairment are expected to utilize doses less than 600 mg twice daily based on the study results and the positive data in cognition previously demonstrated in lower doses.

Completion of clinical trials may take several years or more, but the length of time can vary substantially according to a number of factors, including the type, complexity, novelty and intended use of a drug candidate. The cost of clinical trials, and therefore the amount and timing of our capital requirements, may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others:

- the number of sites included in the trials;
- the length of time required to enroll suitable patient subjects;
- the number of patients that participate in the trials;

- the duration of patient follow-up that seems appropriate in view of results; and
- the efficacy and safety profile of the drug candidate.

We could incur increased clinical development costs if we experience delays in clinical trial enrollment, delays in the evaluation of clinical trial results or delays in regulatory approvals. In addition, we face significant uncertainty with respect to our ability to enter into strategic collaborations with respect to our drug candidates. As a result of these factors, it is difficult to estimate the cost and length of a clinical trial. We are unable to accurately and meaningfully estimate the cost to bring a product to market due to the variability in length of time to develop and obtain regulatory approval for a drug candidate.

We estimate that clinical trials in our areas of focus are typically completed over the following timelines, but delays can occur for many reasons including those set forth above:

<u>Clinical Phase</u>	<u>Objective</u>	<u>Estimated Completion Period</u>
Phase 1	Establish safety in healthy volunteers and occasionally in patients; study how the drug works, is metabolized and interacts with other drugs	1-2 years
Phase 2	Evaluate efficacy, optimal dosages and expanded evidence of safety	2-3 years
Phase 3	Further evaluate efficacy and safety of the drug candidate in a larger patient population	2-3 years

If we successfully complete Phase 3 clinical trials of a drug candidate, we intend to submit the results of all of the clinical trials for such drug candidate to the FDA to support regulatory approval. Even if any of our drug candidates receive regulatory approval, we may still be required to perform lengthy and costly post-marketing studies.

A major risk associated with the timely completion and commercialization of our drug candidates is the ability to confirm safety and efficacy based on the data of long-term clinical trials. We cannot be certain that any of our drug candidates will prove to be safe or effective, will receive regulatory approvals or will be successfully commercialized. In order to achieve marketing approval, the FDA or foreign regulatory agencies must conclude that our clinical data establishes the safety and efficacy of our drug candidates. If our clinical-stage drug candidates are not successfully developed, future results of operations may be adversely affected.

We do not budget or manage our research and development costs by project on a fully allocated basis. Consequently, fully loaded research and development costs by project are not available. We use our employee and infrastructure resources across several projects, and many of our costs are not attributable to an individually-named project but are directed to broadly applicable research projects. As a result, we cannot state precisely the costs incurred for each of our clinical and preclinical projects on a project-by-project basis. We estimate that, from the date we acquired Predix, August 16, 2006 through December 31, 2007, the total payments we made to third-parties for preclinical study support, clinical supplies and clinical trials associated with PRX-08066, PRX-00023, PRX-03140 and PRX-07034 are as follows:

PRX-08066	\$ 5.1 million
PRX-00023	\$12.6 million
PRX-03140	\$ 9.1 million
PRX-07034	\$ 8.5 million

As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will receive cash inflows from the commercialization and sale of a product.

## Financial Results

### *Years ended December 31, 2007 and 2006*

#### *Revenue*

The following table presents revenue and revenue growth (decline) for the years ended December 31, 2007, 2006 and 2005:

	Years Ended December 31,			
	2007	Increase (Decrease)	2006	Increase (Decrease)
	Revenue		Revenue	
Product development revenue . .	\$10,239,120	252%	\$2,909,402	(31)%
Royalty revenue . . . . .	1,017,669	(37)%	1,603,230	(31)%
License fee revenue . . . . .	3,703,260	142%	1,527,910	131%
Total . . . . .	<u>\$14,960,049</u>	148%	<u>\$6,040,542</u>	(16)%

Our revenue to date has consisted principally of product development revenue under our collaboration agreements with GlaxoSmithKline, Cystic Fibrosis Foundation Therapeutics, Incorporated, or CFFT, and Bayer Schering Pharma AG, Germany (for imaging research and development programs); from license fee revenue relating to our agreements with Amgen, GlaxoSmithKline, Bayer Schering Pharma AG, Germany, CFFT, Covidien and Bracco; and from royalties related to our agreements with Bracco and Bayer Schering Pharma AG, Germany. Royalties from Bracco concluded in the second quarter of 2007.

Product development revenue increased 252% in the year ended December 31, 2007 compared to the prior year primarily as a result of \$7.8 million of milestones achieved from our collaboration agreements with GlaxoSmithKline and CFFT, as well as revenue from reimbursed research costs earned under both of these agreements. The increases in revenue for 2007 was partially offset by decreases in revenue due to the completion of our imaging research programs with Bayer Schering Pharma AG, Germany in 2006, as well as lower development revenue for Vasovist.

The decrease in royalty revenue of 37% in the year ended December 31, 2007 compared to the prior year was primarily due to a reduction in royalties on sales of MultiHance by Bracco due to the expiration of patents. Future royalty revenue will consist solely of royalties on sales of Vasovist outside of the United States and Primovist, which are not expected to be significant.

License fee revenue increased 142% in the year ended December 31, 2007 compared to the prior year primarily as a result of an increase of \$2.5 million in the recognition of deferred revenue from the Amgen and GlaxoSmithKline collaboration agreements. Partially offsetting this increase was a decrease in revenue of \$0.2 million from the recognition of the Bracco license fee as this fee was fully recognized by June 2006. The deferred revenue from our Amgen agreement was fully recognized in October 2007 when our research obligation ended.

#### *Research and Development Expense*

Research and development expense of \$57.5 million for the year ended December 31, 2007 reflects an increase of 119% from the prior year. The increase in research and development expense during 2007 was primarily due to an increase in third-party expenses associated with our clinical development programs of \$19.7 million during the twelve months ended December 31, 2007, as well as increased costs for the preclinical programs and internal costs which began after the Predix acquisition was completed on August 16, 2006. Clinical program costs incurred in the current year include costs for the Phase 2b clinical trial of PRX-00023 for depression, costs incurred for the recently completed Phase 2a clinical trial of PRX-03140 for the treatment of Alzheimer's disease, costs incurred for the completed Phase 2a clinical trial of PRX-08066 for the treatment of pulmonary hypertension in association with chronic obstructive pulmonary disease, and costs incurred for the completed Phase 1b multiple ascending dose clinical trials of PRX-07034 for the treatment of obesity and cognitive impairment. The increased costs as described above were partially offset by

the discontinuation of spending on imaging programs subsequent to the merger with Predix. Spending during 2007 and 2006 for Vasovist primarily involved costs related to our appeal to the FDA and was not significant.

#### *In-Process Research and Development Charge*

In connection with our acquisition of Predix in August of 2006, we incurred a nonrecurring charge of \$123.5 million for in-process research and development. The in-process research and development charge represented the fair value of purchased in-process technology of Predix for research projects that, as of the closing date of the merger, had not reached technological feasibility and have no alternative future use. The in-process research and development primarily represents the fair value of the following drug candidates: PRX-00023 (\$70.9 million) that, as of the date of the merger, was in a Phase 3 clinical trial for the treatment of generalized anxiety disorder; PRX-03140 (\$23.5 million) that, as of the date of the merger had completed Phase 1 clinical trials for the treatment of Alzheimer's disease; PRX-08066 (\$20.2 million) that, as of the date of the merger, had entered a Phase 2 clinical trial for the treatment of pulmonary hypertension in association with COPD; and PRX-07034 (\$8.9 million) that, as of the date of the merger, had entered a Phase 1 clinical trial for the treatment of obesity. Since the merger we have spent, and anticipate that we will continue to spend, a significant portion of our research and development budget on advancing these four drug candidates through additional clinical trials.

#### *General and Administrative Expense*

General and administrative expense of \$20.1 million for the year ended December 31, 2007 reflects an increase of 64% from the prior year. The increase in general and administrative expense during 2007 includes incremental costs associated with the increase in personnel and infrastructure relating to the Predix business that was acquired on August 16, 2006 and higher legal expenses for patent-related matters and general corporate items due to the increased complexity of the post-merger entity. In addition, 2007 includes nonrecurring legal and accounting costs of approximately \$5.7 million associated with our stock option investigation that was completed in the first quarter of 2007.

#### *Royalty Expense*

Royalty expense of \$0.6 million for the year ended December 31, 2007 reflects a decrease of approximately \$0.5 million from the prior year. The 2007 expense primarily consists of royalty payments made to Ramot at Tel Aviv University Ltd. resulting from the receipt of milestone payments in 2007 from our collaboration partners. The 2006 expense primarily consists of the royalty payment to Ramot resulting from the payments we received from the execution of the GlaxoSmithKline agreement in December 2006.

All of our current clinical-stage therapeutic drug candidates, PRX-00023, PRX-03140, PRX-08066 and PRX-07034, were, at least in part, identified, characterized or developed using the licensed technology acquired from Ramot, and we are required to make payments to Ramot, as described below, as and when rights to any such drug candidates are ever sublicensed or any such drug candidates are commercialized. In addition, we have used the licensed technology in all of our preclinical-stage programs, and would expect to make payments to Ramot if rights to any drug candidates were ever commercialized from any of these programs.

We also are required to share between 5% and 10% of the consideration we receive from parties to whom we grant sublicenses of rights in the Ramot technology or sublicenses of rights in products identified, characterized or developed with the use of such technology and between 2% and 4% of consideration we receive from performing services using such technology. We would also be required to pay Ramot royalties on sales of products developed with the use of such technology.

#### *Restructuring Costs*

Restructuring costs amounted to \$0.4 million and \$0.6 million for the years ended December 31, 2007 and 2006, respectively. Restructuring costs for the twelve months ended December 31, 2007 include a restructuring charge of \$0.5 million recorded in the second quarter for the consolidation of a leased laboratory

facility in Cambridge, Massachusetts into our Lexington, Massachusetts facility. The charge consisted primarily of future lease costs through the end of 2007. The consolidation was completed during the second quarter of 2007. In addition, during the second quarter of 2007, we recorded a reduction of our 2006 restructuring charge in the amount of \$0.1 million resulting from a reduction in the amount of space leased at our former headquarters location in Cambridge, Massachusetts.

Restructuring costs of \$0.6 million for the twelve months ended December 31, 2006 include a charge of \$0.2 million recorded in the third quarter for the consolidation of our former Cambridge, Massachusetts headquarters into our Lexington, Massachusetts facility. The charge primarily consists of future lease payments through the end of 2007 and the write-off of leasehold improvements. In addition, in the first quarter of 2006, we recorded a charge of \$0.4 million that represented additional costs related to the December 2005 restructuring whereby we reduced our workforce by 48 employees, or approximately 50%, in response to the FDA's second approvable letter regarding Vasovist. The reductions, which were completed in January 2006, affected both the research and development and the general and administrative areas of the company and included severance costs as well as costs related to vacating certain leased space and the write-off of leasehold improvements.

#### *Interest and Other Income*

Interest and other income of \$4.9 million for the twelve months ended December 31, 2007 represents a decrease of 11% from 2006. The decrease in interest income was primarily due to lower levels of cash and investments available to invest due to cash being used to fund operations, partially offset by \$0.6 million received in 2007 from the settlement of a contract dispute.

#### *Interest Expense*

Interest expense of \$4.1 million for the year ended December 31, 2007 represents a decrease of 20% from 2006. The decrease in interest expense is primarily due to a \$0.8 million decrease in the value of the embedded derivative relating to the stock portion of the milestone payable to the former shareholders of Predix, partially offset by increased interest expense relating to the cash portion of the milestone payment. Prior to the payment of the milestone to the former shareholders of Predix in October 2007, we recorded interest expense on the milestone at the greater of the stated rate of 10% or the value of the embedded derivative included in the milestone, which provided for the milestone payment to be paid in shares of our common stock based on 75% of the 30-day average closing price of our common stock ending on October 19, 2007. This embedded derivative was recorded at its fair value and changes in the fair value were recorded as interest expense.

#### *Provision for Income Taxes*

The provision for income taxes represents income taxes required to be withheld in Italy on Bracco royalties for MultiHance sales. Royalties on these sales were discontinued in the second quarter of 2007.

#### *Years ended December 31, 2006 and 2005*

##### *Revenue*

Product development revenue decreased 31% in the year ended December 31, 2006 compared to the prior year primarily as a result of decreased reimbursement of imaging research and development costs due to our shift in focus from imaging agents to therapeutic drug candidates, and the completion of the clinical trials for Vasovist. This decrease was partially offset by revenue of approximately \$0.9 million in 2006 from the CFFT program.

The decrease in royalty revenue of 31% for the year ended December 31, 2006 compared to the prior year resulted from a reduction in the royalty rate on sales of MultiHance by Bracco as total qualified sales of MultiHance exceeded a level established in the agreement and lower overall royalty-eligible sales due to the

expiration of certain patents related to the sublicense with Bracco. Royalties from sales of Vasovist in Europe, which were first received in the third quarter of 2006, were less than \$0.1 million.

License fee revenue increased 131% in the year ended December 31, 2006 compared to the prior year primarily as a result of the recognition of deferred revenue from the Amgen and GlaxoSmithKline agreements. Partially offsetting this increase was a decrease in revenue from the recognition of the Bracco license fee as this fee was fully recognized by June 2006.

#### *Research and Development Expense*

Research and development expense of \$26.3 million for the year ended December 31, 2006 reflects an increase of 44% from the prior year. The increase in research and development expense during 2006 is primarily due to external expenses of \$7.8 million associated with the clinical development programs as well as costs for the preclinical programs and internal costs which began after the Predix acquisition was completed on August 16, 2006. In connection with the Predix acquisition, we shifted our focus away from the discovery and development of imaging agents to the discovery and development of therapeutics. At the time of the merger, Predix had four drug candidates in the clinic. Clinical program costs incurred since the acquisition included completion of a Phase 3 clinical trial for generalized anxiety disorder with PRX-00023; costs incurred for the completion of the Phase I clinical trial and ongoing Phase 2a clinical trial of PRX-03140 for the treatment of Alzheimer's disease, costs incurred for the ongoing Phase 2a clinical trial of PRX-08066 for the treatment of pulmonary hypertension in association with chronic obstructive pulmonary disease, and costs incurred for completion of a single ascending dose clinical trial and the cost of the ongoing Phase I multiple ascending dose clinical trial of PRX-07034 for the treatment of obesity and cognitive impairment. In addition, we recognized non-cash expense of approximately \$2.7 million resulting from our recognition of stock compensation related to the implementation of SFAS 123(R) in 2006 as compared to a credit of \$1.8 million in 2005 based on the accounting for stock compensation under APB 25. The credit in 2005 was primarily due to a reduction in expense for options that were subject to variable accounting as our stock price declined during 2005 as compared to 2004. In addition, in the third quarter of 2006 we recorded a charge of approximately \$0.9 million for our obligation under the settlement agreement reached with Dr. Prince in 2003 to provide him with Vasovist product for the life of the agreement. The increased costs in 2006 as described above were partially offset by lower levels of spending on our imaging programs. In addition, we are no longer conducting preclinical or clinical studies on any imaging product candidates. Spending during 2006 for Vasovist primarily involved consulting costs related to our appeal to the FDA.

#### *General and Administrative Expense*

General and administrative expense of \$12.3 million for the year ended December 31, 2006 reflects an increase of 28% from the prior year. The increase in general and administrative expense during 2006 is primarily due to increased costs associated with the increase in personnel and infrastructure relating to the Predix business that was acquired on August 16, 2006. In addition, legal expenses for patent-related matters and general corporate items increased due to the increasing complexity of the post merger entity. In addition, we recognized non-cash expense of approximately \$1.5 million resulting from our recognition of stock compensation related to the implementation of SFAS 123(R) as compared to a credit of \$1.2 million in 2005 based on the accounting for stock compensation under APB 25. The credit in 2005 was primarily due to a reduction in expense for options that were subject to variable accounting as our stock price declined during 2005 as compared to 2004.

#### *Royalty Expense*

Royalty expense of \$1.1 million for the year ended December 31, 2006 reflects an increase of approximately \$1.0 million from the prior year. The increase in royalty expense during 2006 is primarily due to the royalty payments made to Ramot at Tel Aviv University Ltd. resulting from the payments we received from GlaxoSmithKline in December 2006 relating to our agreement with them. In connection with the GlaxoSmithKline agreement, we received an upfront payment and proceeds from an equity investment in our

common stock. We paid Ramot a royalty of approximately \$1.0 million relating to the GlaxoSmithKline upfront payment.

#### *Restructuring Costs*

Restructuring costs amounted to \$0.6 million and \$1.0 million for the years ended December 31, 2006 and 2005, respectively. The costs incurred in 2005 primarily consisted of severance and benefits relating to the 2005 reduction in force. In December 2005, we reduced our workforce by 48 employees, or approximately 50%, in response to the FDA's second approvable letter regarding Vasovist. The reductions, which were completed in January 2006, affected both the research and development and the general and administrative areas of the Company. The 2006 costs included approximately \$0.4 million related to the 2005 restructuring plan for additional severance costs as well as costs related to vacating certain leased space and the write-off of leasehold improvements. In addition, in the third quarter of 2006, we recorded additional restructuring charges of \$0.2 million for facility exit costs related to the consolidation of our Cambridge, MA headquarters into the former Predix headquarters in Lexington, MA. These costs primarily consist of future lease payments through the end of 2007 and the write-off of leasehold improvements.

#### *Interest and Other Income*

Interest and other income of \$5.5 million for the twelve months ended December 31, 2006 represents an increase of 33% from 2005. The increase in interest and other income was primarily due to higher interest rates on our invested cash, cash equivalents and marketable securities during the period.

#### *Interest Expense*

Interest expense of \$5.1 million for the year ended December 31, 2006 represents an increase of 40% from 2005. The increase in interest expense is primarily the result of \$1.4 million of interest related to the \$15.0 million milestone payment due to the former Predix stockholders on October 29, 2007. The interest expense on the milestone primarily represents the increase in value from the date of acquisition of the embedded derivative included in the merger consideration payable which provides for the milestone payment to be paid in shares of our common stock based on 75% of the 30-day average closing price of our common stock ending on the trading day that is ten days prior to the payment date. This embedded derivative is recorded at its fair value and changes in the fair value are recorded as interest expense. Under the terms of the merger agreement, if the milestone cannot be paid in shares of our common stock due to terms of the agreement, the payment plus 10% interest will be made in cash. The increase in interest expense in 2006 was partially offset by lower interest expense on our prior loan facility with Bayer Schering Pharma AG, Germany as that facility was terminated in January 2006.

#### *Provision for Income Taxes*

The provision for income taxes represents Italian income taxes related to the Bracco agreement. The amounts represent Italian income taxes required to be withheld on Bracco royalties for MultiHance sales.

#### **Liquidity and Capital Resources**

Our principal sources of liquidity consist of cash, cash equivalents and available-for-sale marketable securities of \$61.1 million at December 31, 2007 as compared to \$109.5 million at December 31, 2006. The decrease in cash, cash equivalents and available-for-sale marketable securities of \$48.4 million was primarily attributable to funding of ongoing operations during the fiscal year, as well as paying the second and final milestone payment for the Predix merger.

We used approximately \$57.1 million of cash to fund operating activities for the twelve months ended December 31, 2007, as compared to a use of \$15.6 million for the same period in 2006. The increase in the cash used for operating activities in 2007 is primarily due to an increase in the net loss in 2007 compared to 2006 (after excluding the \$123.5 non-cash charge in 2006 for acquired in-process research and development) and the receipt in 2006 of a \$17.5 million payment from GlaxoSmithKline that was recorded as deferred

revenue. The net use of cash to fund operations for the twelve months ended December 31, 2007 primarily resulted from the net loss of \$62.8 million, which was partially offset by an increase of \$2.0 million in accounts payable and accrued expenses largely resulting from increased clinical activity at year end. During the twelve months ended December 31, 2007, we also received approximately \$3.3 million of landlord allowances related to the laboratory construction at our Lexington, Massachusetts facility. The net cash used to fund operations during the twelve months ended December 31, 2006 of \$15.6 million was primarily due to the net loss incurred of \$157.4 million that included a non-cash charge for the write-off of in-process research and development of \$123.5 million from the Predix merger. During 2006, we also received \$17.5 million as an up-front payment upon signing the GlaxoSmithKline agreement and paid down accruals by approximately \$5.9 million which primarily related to liabilities assumed in the merger with Predix.

Our investing activities provided \$20.5 million of cash during the twelve months ended December 31, 2007 as compared to \$35.0 million of cash used during the same period in 2006. Investing activities in 2007 primarily consisted of the net redemption of \$29.6 million of marketable securities to fund operating activities, \$4.2 million of capital expenditures primarily related to the build out of laboratory space at our Lexington facility and \$5.3 million for the cash payment of the principal portion of the second milestone for the Predix merger. Investing activities in 2006 primarily consisted of the net purchase of \$26.3 million of marketable securities and \$7.1 million for the first milestone payment for the Predix merger, net of cash acquired.

Our financing activities provided \$15.5 million of cash during the twelve months ended December 31, 2007, primarily due to \$15.0 million of proceeds received from the private placement of our common stock in November 2007. Financing activities provided \$8.5 million during the twelve months ended December 31, 2006 due to the sale of \$17.5 million of common stock to GlaxoSmithKline, which was partially offset by the payment of \$9.5 million of bridge loans assumed in the Predix merger.

Our primary sources of cash include quarterly payments from CFFT and GlaxoSmithKline for research services and monthly interest income on our cash, cash equivalents and available-for-sale marketable securities. We do not expect the royalties received on non-United States sales of Vasovist to be significant in the near term. Other potential cash inflows include future milestone and option payments from our current strategic collaborators, GlaxoSmithKline, Amgen, and CFFT. Because of anticipated spending for the continued development of our preclinical and clinical compounds, we do not expect positive cash flow from operating activities for at least the next several years.

Known outflows, in addition to our ongoing research and development and general and administrative expenses, include interest on our \$100.0 million convertible notes at a rate of 3% payable semi-annually on June 15 and December 15 and a milestone payment of \$2.5 million owed to Covidien, in the event the FDA approves Vasovist.

The following table represents payments due under contractual obligations as of December 31, 2007:

Contractual Obligations	Total	Payments Due by Period			
		Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
Long-term debt obligations, including interest payments . .	\$110,500,000	\$3,000,000	\$ 6,000,000	\$101,500,000	\$ —
Operating lease obligations . . . .	15,380,260	2,698,410	5,035,970	3,853,363	3,792,517
Capital lease obligations . . . . .	406,489	208,478	198,011	—	—
Unconditional purchase obligations . . . . .	1,566,379	1,566,379	—	—	—
Other long-term liabilities . . . . .	2,905,000	385,000	280,000	280,000	1,960,000
Total . . . . .	<u>\$130,758,128</u>	<u>\$7,858,267</u>	<u>\$11,513,981</u>	<u>\$105,633,363</u>	<u>\$5,752,517</u>

We estimate that cash, cash equivalents and marketable securities on hand as of December 31, 2007 and anticipated revenue we will earn in 2008 will fund our operations through the first quarter of 2009. Our future liquidity and capital requirements will depend on numerous factors, including the following: the progress and

scope of clinical and preclinical trials; the timing and costs of filing future regulatory submissions; the timing and costs required to receive both U.S. and foreign governmental approvals; the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights; the extent to which our products, if any, gain market acceptance; the timing and costs of product introductions; the extent of our ongoing and new research and development programs; the costs of training physicians to become proficient with the use of our potential products; and, if necessary, once regulatory approvals are received, the costs of developing marketing and distribution capabilities. In addition, if holders of our convertible senior notes require redemption of the notes, we would be required to repay \$100.0 million, plus accrued and unpaid interest, on June 15, 2011, 2014 and 2019 and upon certain other designated events under the notes, which include a change of control or termination of trading of our common stock on the NASDAQ Global Market. We may need to raise substantial additional funds to cover our future capital requirements through equity or debt financings, strategic alliances or otherwise. We cannot assure you that additional financing will be available on terms favorable to us, or at all. If adequate funds are not available or are not available on acceptable terms, when we desire them, our ability to fund our operations, take advantage of unanticipated opportunities or otherwise respond to competitive pressures would be significantly limited.

#### **ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK**

The objective of our investment activities is to preserve principal, while at the same time maximizing yields without significantly increasing risk. To achieve this objective, in accordance with our investment policy, we invest our cash in a variety of financial instruments, principally restricted to government-sponsored enterprises, high-grade bank obligations, high-grade corporate bonds, high-grade asset-backed securities, and certain money market funds. These investments are denominated in U.S. dollars.

Investments in both fixed rate and floating rate interest earning instruments carry a degree of interest rate risk. Fixed rate securities may have their fair market value adversely impacted due to a rise in interest rates, while floating rate securities may produce less income than expected if interest rates fall. Due in part to these factors, our future investment income may fall short of expectations due to changes in interest rates or we may suffer losses in principal if forced to sell securities that have seen a decline in market value due to changes in interest rates. A hypothetical 10% increase or decrease in interest rates would result in an insignificant change in the fair market value of our total portfolio at December 31, 2007.

#### **ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

<u>Index to Consolidated Financial Statements</u>	<u>Number</u>
Report of Independent Registered Public Accounting Firm .....	F-2
Consolidated Financial Statements:	
Consolidated Balance Sheets .....	F-3
Consolidated Statements of Operations .....	F-4
Consolidated Statements of Stockholders' Equity (Deficit) .....	F-5
Consolidated Statements of Cash Flows .....	F-6
Notes to Consolidated Financial Statements .....	F-7

#### **ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE**

There have been no disagreements with accountants on accounting or financial disclosure matters during our two most recent fiscal years.

#### **Item 9A. CONTROLS AND PROCEDURES**

##### **Management's Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Exchange Act

Rules 13a-15(e)) as of December 31, 2007. Based on this evaluation, our chief executive officer and chief financial officer concluded that, as of December 31, 2007, our disclosure controls and procedures were effective in providing reasonable assurance that information required to be disclosed by us in reports that we file or submit under the Exchange Act is recorded, processed, summarized, reported and accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate to allow timely decisions regarding required disclosure.

### **Management's Annual Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) under the Securities Exchange Act of 1934, as amended, as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflects transactions in and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2007. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework.

Based on our assessment, management concludes that, as of December 31, 2007, our internal control over financial reporting is effective based on those criteria.

The company's independent registered public accounting firm, Ernst & Young LLP, has audited the effectiveness of the company's internal control over financial reporting as of December 31, 2007, as stated in their report that appears on page 61 of this Annual Report on Form 10-K.

### **Changes in Internal Controls over Financial Reporting**

There was no change in our internal control over financial reporting that occurred during the fourth quarter of 2007 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

### **Item 9B. OTHER INFORMATION**

None.

## **Report of Independent Registered Public Accounting Firm**

The Board of Directors and Shareholders of  
EPIX Pharmaceuticals, Inc.

We have audited EPIX Pharmaceuticals Inc.'s internal control over financial reporting as of December 31, 2007, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). EPIX Pharmaceuticals Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Controls. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, EPIX Pharmaceuticals Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2007, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the accompanying consolidated balance sheets of EPIX Pharmaceuticals, Inc. as of December 31, 2007 and 2006, and the related statements of operations, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2007 and our report dated March 13, 2008 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts  
March 13, 2008

### **PART III**

#### **ITEM 10. *DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2007.

#### **ITEM 11. *EXECUTIVE COMPENSATION***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2007.

#### **ITEM 12. *SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2007.

#### **ITEM 13. *CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2007.

#### **ITEM 14. *PRINCIPAL ACCOUNTING FEES AND SERVICES***

The information required under this item is incorporated herein by reference to the Company's definitive proxy statement pursuant to Regulation 14A, which proxy statement will be filed with the Securities and Exchange Commission not later than 120 days after the close of the Company's fiscal year ended December 31, 2007.

### **PART IV**

#### **ITEM 15. *EXHIBITS, FINANCIAL STATEMENT SCHEDULES***

##### **Item 15(a).**

The following documents are filed as part of this Annual Report on Form 10-K

##### **Item 15(a) (1) and (2).**

See "Index to Financial Statements" at Item 8 to this Annual Report on Form 10-K. Financial statement schedules have not been included because they are not applicable or the information is included in the financial statements or notes thereto.

**Item 15(a) (3). Exhibits**

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

<u>Exhibit Number</u>	<u>Description</u>
3.1@	Restated Certificate of Incorporation of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
3.2@	Amended and Restated By-Laws of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2007 and incorporated herein by reference.
4.1@	Specimen certificate for shares of Common Stock of the Company. Filed as Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.2@	Indenture dated as of June 7, 2004 between the Company and U.S. Bank National Association as Trustee, relating to 3% Convertible Senior Notes due June 15, 2024. Filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed June 7, 2004 and incorporated herein by reference.
4.3@	Warrant issued to RRD International, LLC. Filed as Exhibit 4.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.4@	Warrant issued to General Electric Capital Corporation. Filed as Exhibit 4.4 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.1@+	Amended and Restated License Agreement between the Company and The General Hospital Corporation dated July 10, 1995. Filed as Exhibit 10.14 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.2@#	Amended and Restated 1992 Incentive Plan. Filed as Appendix A to the Company's 2005 Definitive Proxy Statement on Schedule 14A filed April 29, 2005 and incorporated herein by reference.
10.3@#	Form of Incentive Stock Option Certificate. Filed as Exhibit 10.29 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.4@#	Form of Nonstatutory Stock Option Certificate. Filed as Exhibit 10.30 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.5@#	Amended and Restated 1996 Director Stock Option Plan. Filed as Appendix B to the Company's 2005 Definitive Proxy Statement on Schedule 14A filed April 29, 2005 and incorporated herein by reference.
10.6*++	Amended and Restated Strategic Collaboration Agreement dated as of June 9, 2000, among the Company, Mallinckrodt Inc. (a Delaware corporation) and Mallinckrodt Inc. (a New York corporation).
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10.8*	Amendment No. 1 dated as of December 22, 2000 to the Strategic Collaboration Agreement, dated as of June 9, 2000, between the Company and Schering Aktiengesellschaft.
10.9@	Intellectual Property Agreement by and between the Company and Dr. Martin R. Prince, dated November 17, 2003. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 18, 2003 and incorporated herein by reference.
10.10@#	Description of Director Compensation Arrangements. Filed with the Company's Current Report on Form 8-K filed June 4, 2007 and incorporated herein by reference.
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10.15@++	Amended and Restated License Agreement between Ramot at Tel Aviv University Ltd., Company Registration No. 51-066714-0 and Predix Pharmaceuticals Holdings, Inc., dated as of May 20, 2004. Filed as Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.16@++	Research, Development and Commercialization Agreement between Predix Pharmaceuticals Holdings, Inc. and Cystic Fibrosis Foundation Therapeutics, Incorporated, dated as of March 7, 2005. Filed as Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.17@++	License Agreement between Amgen Inc. and Predix Pharmaceuticals Holdings, Inc., dated as of July 31, 2006. Filed as Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.18@	Lease by and between Trustees of 4 Maguire Road Realty Trust and Predix Pharmaceuticals Holdings, Inc., dated as of January 30, 1998, as amended by First Amendment to Lease by and between Trustees of 4 Maguire Road Realty Trust and EPIX Delaware, Inc., dated as of August 31, 2006. Filed as Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.19@	Lease Agreement by and between 150 College Road, LLC and Physiome Sciences, Inc., dated as of December 21, 2000, as amended. Filed as Exhibit 10.7 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.20@	Sublease by and between Predix Pharmaceuticals Holdings, Inc. and Novo Nordisk Pharmaceuticals, Inc., dated as of December 12, 2003. Filed as Exhibit 10.8 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.21@	Unprotected Lease Agreement between "Emed" Real Estate Development and Investments Company Ltd. and Predix Pharmaceuticals Ltd., dated as of September 26, 2004. Filed as Exhibit 10.9 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.22@#	Predix Pharmaceuticals, Inc. Employment Agreement between Predix Pharmaceuticals, Inc. and Chen Schor, dated as of November 23, 2003. Filed as Exhibit 10.13 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.23@#	Bio-I.T. (Bio Information Technologies) Ltd. Employment Agreement between Bio-I.T. (Bio Information Technologies) Ltd. and Dr. Oren Becker, dated as of October 31, 2000. Filed as Exhibit 10.14 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.24@++	Development and License Agreement among SmithKline Beecham Corporation, doing business as GlaxoSmithKline, Glaxo Group Limited and the Company, dated as of December 11, 2006. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K/A filed January 18, 2007 and incorporated herein by reference.
10.25@	Stock Purchase Agreement among the Company, Glaxo Group Limited and SmithKline Beecham Corporation, doing business as GlaxoSmithKline, dated as of December 11, 2006. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K/A filed January 18, 2007 and incorporated herein by reference.
10.26@	First Amendment to License Agreement between Amgen Inc. and the Company, dated as of March 20, 2007. Filed as Exhibit 10.52 to the Company's Annual Report on Form 10-K for the year ended December 31, 2006 and incorporated herein by reference.
10.27@#	Employment Agreement between the Company and Kimberlee C. Drapkin, dated as of March 26, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed March 29, 2007 and incorporated herein by reference.

<u>Exhibit Number</u>	<u>Description</u>
10.28@#	Employment Agreement between the Company and Michael G. Kauffman, M.D., Ph.D., dated as of March 27, 2007. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed March 29, 2007 and incorporated herein by reference.
10.29@#	Release Agreement by and between the Company and Oren Becker, dated as of April 5, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed April 6, 2007 and incorporated herein by reference.
10.30@#	2006 Employee Stock Purchase Plan. Filed as Appendix A to the Company's 2007 Definitive Proxy Statement on Schedule 14A filed April 30, 2007 and incorporated herein by reference.
10.31@++	First Amendment to Amended and Restated License Agreement between the Company and Ramot at Tel Aviv University Ltd., dated as of June 13, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed June 15, 2007 and incorporated herein by reference.
10.32@#	Employment Agreement between the Company and Andrew Uprichard, MD, dated as of August 9, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed August 10, 2007 and incorporated herein by reference.
10.33@++	Third Amendment to Research, Development and Commercialization Agreement between the Company and Cystic Fibrosis Foundation Therapeutics, Incorporated, dated as of November 1, 2007. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 7, 2007 and incorporated herein by reference.
10.34@	Form of Securities Purchase Agreement dated November 9, 2007 between the Company and each of the purchasers listed on Exhibit A thereto. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed November 15, 2007 and incorporated herein by reference.
10.35@#	Form of Restricted Stock Unit Agreement under the Amended and Restated 1992 Incentive Plan. Filed as Exhibit 10.1 to the Company's Current Report on Form 8-K filed February 22, 2008 and incorporated herein by reference.
10.36@#	Form of Restricted Stock Unit Agreement under the Amended and Restated 2003 Stock Option and Incentive Plan. Filed as Exhibit 10.2 to the Company's Current Report on Form 8-K filed February 22, 2008 and incorporated herein by reference.
12.1*	Ratio of Earnings to Fixed Charges.
21.1@	Subsidiaries of the Company. Filed as Exhibit 21.1 to the Company's Annual Report on Form 10-K for the year ended December 31, 2006 and incorporated herein by reference.
23.1*	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on signature page to this Annual Report on Form 10-K).
31.1*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Michael G. Kauffman.
31.2*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002 for Kim Cobleigh Drapkin.
32*	Certification pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, U.S. Code).

@ Incorporated by reference as indicated.

\* Filed herewith.

# Identifies a management contract or compensatory plan or agreement in which an executive officer or director of the Company participates.

+ Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

++ Certain confidential material contained in the document has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

## SIGNATURES

Pursuant to the requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

EPIX PHARMACEUTICALS, INC.

By: /s/ KIM COBLEIGH DRAPKIN

Kim Cobleigh Drapkin, CPA  
Chief Financial Officer  
(Principal Financial and Accounting Officer)

March 17, 2008

## POWER OF ATTORNEY

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Michael G. Kauffman, M.D., Ph.D., Andrew C.G. Uprichard, M.D. and Kim Cobleigh Drapkin, CPA, jointly and severally, his or her attorney-in-fact, with the power of substitution, for him or her in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes, may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1934, this Report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ MICHAEL G. KAUFFMAN</u> Michael G. Kauffman, M.D., Ph.D.	Chief Executive Officer and Director (Principal Executive Officer)	March 17, 2008
<u>/s/ KIM COBLEIGH DRAPKIN</u> Kim Cobleigh Drapkin, CPA	Chief Financial Officer (Principal Financial and Accounting Officer)	March 17, 2008
<u>/s/ FREDERICK FRANK</u> Frederick Frank	Chairman of the Board of Directors	March 17, 2008
<u>/s/ PATRICK J. FORTUNE</u> Patrick J. Fortune, Ph.D.	Director	March 17, 2008
<u>/s/ MICHAEL GILMAN</u> Michael Gilman, Ph.D.	Director	March 17, 2008
<u>/s/ MARK LEUCHTENBERGER</u> Mark Leuchtenberger	Director	March 17, 2008
<u>/s/ ROBERT J. PEREZ</u> Robert J. Perez	Director	March 17, 2008
<u>/s/ GREGORY D. PHELPS</u> Gregory D. Phelps	Director	March 17, 2008
<u>/s/ IAN F. SMITH</u> Ian F. Smith, CPA, ACA	Director	March 17, 2008

## EXHIBIT INDEX

<u>Exhibit Number</u>	<u>Description</u>
3.1@	Restated Certificate of Incorporation of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
3.2@	Amended and Restated By-Laws of the Company. Filed as Exhibit 3.1 to the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2007 and incorporated herein by reference.
4.1@	Specimen certificate for shares of Common Stock of the Company. Filed as Exhibit 4.1 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.2@	Indenture dated as of June 7, 2004 between the Company and U.S. Bank National Association as Trustee, relating to 3% Convertible Senior Notes due June 15, 2024. Filed as Exhibit 4.1 to the Company's Current Report on Form 8-K filed June 7, 2004 and incorporated herein by reference.
4.3@	Warrant issued to RRD International, LLC. Filed as Exhibit 4.3 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
4.4@	Warrant issued to General Electric Capital Corporation. Filed as Exhibit 4.4 to the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2006 and incorporated herein by reference.
10.1@+	Amended and Restated License Agreement between the Company and The General Hospital Corporation dated July 10, 1995. Filed as Exhibit 10.14 to the Company's Registration Statement on Form S-1 filed December 10, 1996 (File No. 333-17581) and incorporated herein by reference.
10.2@#	Amended and Restated 1992 Incentive Plan. Filed as Appendix A to the Company's 2005 Definitive Proxy Statement on Schedule 14A filed April 29, 2005 and incorporated herein by reference.
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# Identifies a management contract or compensatory plan or agreement in which an executive officer or director of the Company participates.

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**EPIX PHARMACEUTICALS, INC.**  
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## **REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Stockholders  
EPIX Pharmaceuticals, Inc.:

We have audited the accompanying consolidated balance sheets of EPIX Pharmaceuticals, Inc. as of December 31, 2007 and 2006, and the related statements of operations, stockholders' equity(deficit), and cash flows for each of the three years in the period ended December 31, 2007. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of EPIX Pharmaceuticals, Inc. at December 31, 2007 and 2006, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2007, in conformity with U.S. generally accepted accounting principles.

As discussed in Note 2 to the consolidated financial statements, on January 1, 2006, the Company adopted the provisions of Statement of Financial Accounting Standards No. 123(R), Share-Based Payment.

As discussed in Note 11 to the consolidated financial statements, on January 1, 2007, the Company adopted the provisions of FASB Interpretation No. 48, Accounting for Uncertainty in Income Taxes-An Interpretation of FASB Statement No. 109.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of EPIX Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2007, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 13, 2008 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts  
March 13, 2008

**EPIX PHARMACEUTICALS, INC.**  
**CONSOLIDATED BALANCE SHEETS**

	December 31,	
	2007	2006
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents . . . . .	\$ 9,157,973	\$ 30,332,468
Available-for-sale marketable securities . . . . .	51,919,128	79,210,430
Accounts receivable . . . . .	—	46,367
Prepaid expenses and other assets . . . . .	2,162,895	2,575,265
Total current assets . . . . .	63,239,996	112,164,530
Property and equipment, net . . . . .	6,044,886	3,592,570
Other assets . . . . .	3,850,431	4,330,578
Goodwill . . . . .	4,939,814	4,939,814
Total assets . . . . .	<u>\$ 78,075,127</u>	<u>\$ 125,027,492</u>
<b>LIABILITIES AND STOCKHOLDERS' DEFICIT</b>		
Current liabilities:		
Accounts payable . . . . .	\$ 3,539,099	\$ 1,982,032
Accrued expenses . . . . .	8,099,539	7,695,548
Contract advances . . . . .	4,719,201	4,605,079
Merger consideration payable . . . . .	—	18,504,084
Current portion of capital lease obligation . . . . .	179,859	84,633
Deferred revenue . . . . .	1,372,042	3,665,120
Other current liabilities . . . . .	610,867	446,137
Total current liabilities . . . . .	18,520,607	36,982,633
Deferred revenue . . . . .	15,688,296	17,101,165
Capital lease obligation . . . . .	182,748	102,077
Other liabilities . . . . .	4,975,123	2,862,898
Convertible debt . . . . .	100,000,000	100,000,000
Total liabilities . . . . .	139,366,774	157,048,773
Commitments and contingencies (Note 9)		
Stockholders' deficit:		
Preferred Stock, \$0.01 par value, 1,000,000 shares authorized; no shares issued . . . . .	—	—
Common Stock, \$0.01 par value, 100,000,000 shares authorized; 41,353,079 and 32,524,726 shares issued and outstanding at December 31, 2007 and December 31, 2006, respectively . . . . .	413,530	325,247
Additional paid-in-capital . . . . .	346,289,024	312,984,862
Accumulated deficit . . . . .	(408,157,261)	(345,368,698)
Accumulated other comprehensive income . . . . .	163,060	37,308
Total stockholders' deficit . . . . .	(61,291,647)	(32,021,281)
Total liabilities and stockholders' deficit . . . . .	<u>\$ 78,075,127</u>	<u>\$ 125,027,492</u>

See accompanying notes.

**EPIX PHARMACEUTICALS, INC.**  
**CONSOLIDATED STATEMENTS OF OPERATIONS**

	Year ended December 31,		
	2007	2006	2005
Revenues:			
Product development revenue . . . . .	\$ 10,239,120	\$ 2,909,402	\$ 4,195,530
Royalty revenue . . . . .	1,017,669	1,603,230	2,333,384
License fee revenue . . . . .	3,703,260	1,527,910	660,747
Total revenues . . . . .	14,960,049	6,040,542	7,189,661
Operating expenses:			
Research and development . . . . .	57,526,506	26,255,000	18,293,921
Acquired in-process research and development . . . . .	—	123,500,000	—
General and administrative . . . . .	20,051,893	12,257,320	9,586,132
Royalties . . . . .	595,269	1,063,102	98,089
Restructuring . . . . .	350,137	633,238	971,828
Total operating expenses . . . . .	78,523,805	163,708,660	28,949,970
Operating loss . . . . .	(63,563,756)	(157,668,118)	(21,760,309)
Interest and other income . . . . .	4,901,106	5,496,081	4,146,532
Interest expense . . . . .	(4,067,795)	(5,075,848)	(3,613,190)
Loss before provision for income taxes . . . . .	(62,730,445)	(157,247,885)	(21,226,967)
Provision for income taxes . . . . .	58,118	145,313	41,991
Net loss . . . . .	<u><u>\$(62,788,563)</u></u>	<u><u>\$(157,393,198)</u></u>	<u><u>\$(21,268,958)</u></u>
Weighted average shares:			
Basic and diluted . . . . .	<u>33,936,317</u>	<u>20,789,388</u>	<u>15,505,458</u>
Net loss per share, basic and diluted . . . . .	<u><u>\$ (1.85)</u></u>	<u><u>\$ (7.57)</u></u>	<u><u>\$ (1.37)</u></u>

See accompanying notes.

**EPIX PHARMACEUTICALS, INC.**

**CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)**

	<b>Common Stock</b>		<b>Additional Paid-In Capital</b>	<b>Accumulated Deficit</b>	<b>Accumulated Other Comprehensive Income/(loss)</b>	<b>Total Stockholders' Equity (Deficit)</b>
	<b>Shares</b>	<b>Amount</b>				
Balance at December 31, 2004 . . . . .	15,460,103	\$154,601	\$207,274,676	\$(166,706,542)	\$(246,883)	\$ 40,475,852
Issuance of common stock upon exercise of options . . . . .	50,332	503	473,612	—	—	474,115
Issuance of common stock under employee stock purchase plan . . . . .	12,772	128	103,868	—	—	103,996
Stock-based compensation expense . . . . .	—	—	(3,018,396)	—	—	(3,018,396)
Net loss . . . . .	—	—	—	(21,268,958)	—	(21,268,958)
Available-for-sale marketable securities unrealized gain . . . . .	—	—	—	—	180,685	180,685
Comprehensive loss . . . . .	—	—	—	—	—	(21,088,273)
Balance at December 31, 2005 . . . . .	15,523,207	155,232	204,833,760	(187,975,500)	(66,198)	16,947,294
Issuance of common stock under employee stock purchase plan . . . . .	11,165	112	59,863	—	—	59,975
Issuance of common stock upon exercise of options . . . . .	360,018	3,600	454,124	—	—	457,724
Sale of common stock to GlaxoSmithKline . . . . .	3,009,027	30,090	17,469,910	—	—	17,500,000
Stock-based compensation expense . . . . .	—	—	4,203,663	—	—	4,203,663
Cash paid for fractional shares . . . . .	(29)	—	(205)	—	—	(205)
Issuance of common stock in connection with merger . . . . .	13,621,338	136,213	85,963,747	—	—	86,099,960
Net loss . . . . .	—	—	—	(157,393,198)	—	(157,393,198)
Available-for-sale marketable securities unrealized gain . . . . .	—	—	—	—	103,506	103,506
Comprehensive loss . . . . .	—	—	—	—	—	(157,289,692)
Balance at December 31, 2006 . . . . .	32,524,726	325,247	312,984,862	(345,368,698)	37,308	(32,021,281)
Issuance of common stock under employee stock purchase plan . . . . .	54,731	547	203,257	—	—	203,804
Issuance of common stock upon exercise of options . . . . .	361,154	3,612	414,824	—	—	418,436
Sale of common stock . . . . .	5,245,468	52,454	14,957,898	—	—	15,010,352
Stock-based compensation expense . . . . .	—	—	4,775,152	—	—	4,775,152
Issuance of common stock in connection with merger . . . . .	3,167,000	31,670	12,953,031	—	—	12,984,701
Net loss . . . . .	—	—	—	(62,788,563)	—	(62,788,563)
Available-for-sale marketable securities unrealized gain . . . . .	—	—	—	—	125,752	125,752
Comprehensive loss . . . . .	—	—	—	—	—	(62,662,811)
Balance at December 31, 2007 . . . . .	41,353,079	\$413,530	\$346,289,024	\$(408,157,261)	\$ 163,060	\$ (61,291,647)

See accompanying notes.

**EPIX PHARMACEUTICALS, INC.**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**

	Year Ended December 31,		
	2007	2006	2005
Operating activities:			
Net loss	\$ (62,788,563)	\$ (157,393,198)	\$ (21,268,958)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation, amortization and asset write offs	1,959,542	1,548,422	1,188,610
Write-off of acquired in-process research and development	—	123,500,000	—
Stock compensation expense	4,775,152	4,203,663	(3,018,396)
Noncash interest expense (credit) from embedded derivative	(771,592)	936,536	—
Merger consideration interest paid in common stock	975,432	—	—
Amortization of deferred financing costs	510,184	492,337	475,115
Accretion of (discount) premium on available-for-sale securities	(2,582,393)	(593,665)	530,811
Changes in operating assets and liabilities, exclusive of amounts acquired from the merger with Predix:			
Accounts receivable	46,367	852,920	173,259
Prepaid expenses and other current assets	412,370	(282,827)	238,219
Other assets and liabilities	2,421,205	2,073,119	—
Accounts payable	1,557,067	216,567	329,827
Accrued expenses	403,991	(5,892,204)	71,084
Contract advances	114,122	(1,507,470)	(37,464)
Merger consideration payable	(465,517)	465,517	—
Deferred revenue	(3,705,947)	15,741,238	(2,406,099)
Net cash used in operating activities	(57,138,580)	(15,639,045)	(23,723,992)
Investing activities:			
Cash paid for merger with Predix, net of cash acquired	(5,257,707)	(7,142,601)	—
Purchases of marketable securities	(108,710,354)	(124,598,368)	(88,618,059)
Sales or redemptions of marketable securities	138,317,442	98,310,699	127,117,973
Purchases of fixed assets	(4,161,704)	(1,314,374)	(1,215,665)
Other investing activities	293,073	(243,327)	—
Net cash provided by (used in) investing activities	20,480,750	(34,987,971)	37,284,249
Financing activities:			
Proceeds from loan payable from strategic partner	—	—	45,000,000
Repayment of loan payable to strategic partner	—	—	(60,000,000)
Principal payments of notes payable	—	(9,516,380)	—
Principal payments on capital leases	(149,257)	(44,536)	—
Proceeds from sale of common stock	15,010,352	17,500,000	—
Proceeds from stock option exercises	418,436	457,724	474,115
Proceeds from Employee Stock Purchase Plan	203,804	59,975	103,996
Cash paid for fractional shares from reverse stock split	—	(205)	—
Net cash provided by (used in) financing activities	15,483,335	8,456,578	(14,421,889)
Net decrease in cash and cash equivalents	(21,174,495)	(42,170,438)	(861,632)
Cash and cash equivalents at beginning of year	30,332,468	72,502,906	73,364,538
Cash and cash equivalents at end of year	\$ 9,157,973	\$ 30,332,468	\$ 72,502,906
Supplemental cash flow information:			
Cash paid for interest	\$ 3,552,440	\$ 3,383,774	\$ 3,145,883
Cash paid for taxes	\$ 58,118	\$ 145,313	\$ 41,991
Supplemental disclosure of noncash financing and investing activities:			
Milestone obligation paid in common stock	\$ 12,009,268	\$ —	\$ —
Purchases of fixed asset with capital lease	\$ 325,154	\$ —	\$ —

See accompanying notes.

## **EPIX PHARMACEUTICALS, INC.**

### **NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

#### **1. Business**

EPIX Pharmaceuticals, Inc. ("EPIX" or the "Company") is a biopharmaceutical company focused on discovering, developing and commercializing novel pharmaceutical products through the use of proprietary technologies to better diagnose, treat and manage patients. The Company has four internally developed therapeutic product candidates in clinical trials targeting conditions such as depression, Alzheimer's disease, cardiovascular disease and cognitive impairment. The Company's blood-pool imaging agent, Vasovist, is approved for marketing in more than 30 countries outside of the United States. The Company also has collaborations with SmithKline Beecham Corporation (GlaxoSmithKline), Amgen Inc., Cystic Fibrosis Foundation Therapeutics, Incorporated, and Bayer Schering Pharma AG, Germany.

The focus of the Company's therapeutic drug discovery and development efforts is on the two classes of drug targets known as G-protein Coupled Receptors, or GPCRs, and ion channels. GPCRs and ion channels are classes of proteins embedded in the surface membrane of all cells and are responsible for mediating much of the biological signaling at the cellular level. The Company believes its proprietary drug discovery technology and approach addresses many of the inefficiencies associated with traditional GPCR and ion channel-targeted drug discovery. By integrating computer-based, or in silico, technology with in-house medicinal chemistry, the Company believes that it can rapidly identify and optimize highly selective drug candidates. The Company focuses on GPCR and ion channel drug targets whose role in disease has already been demonstrated in clinical trials or in preclinical studies. In each of its four clinical-stage therapeutic programs, the Company used its drug discovery technology and approach to optimize a lead compound into a clinical drug candidate in less than ten months, synthesizing fewer than 80 compounds per program. The Company has moved each of these drug candidates into clinical trials in less than 18 months from lead identification. The Company believes its drug discovery technology and approach enables it to efficiently and cost-effectively discover and develop GPCR and ion channel-targeted drugs.

As of December 31, 2007, the Company had \$61.1 million of cash, cash equivalents and short-term marketable securities. The Company has experienced and continues to experience negative cash flows from operations and it expects to continue to incur net losses in the foreseeable future. The Company believes that it has sufficient cash, along with anticipated revenue the Company will earn in 2008, to meet its funding requirements at least through 2008. There can be no assurance as to the availability of additional financing or the terms upon which additional financing may be available in the future if, and when, it is needed. If adequate funds are not available or are not available on acceptable terms, when the Company desires them, the Company's ability to fund its operations, take advantage of unanticipated opportunities or otherwise respond to competitive pressures would be significantly limited.

#### **2. Significant Accounting Policies**

##### ***Principles of Consolidation***

The consolidated financial statements include the financial statements of the Company and those of its wholly owned subsidiary in Israel. All material intercompany balances and transactions have been eliminated.

##### ***Use of Estimates***

The preparation of financial statements in conformity with accounting principles generally accepted in the U.S. requires the Company to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

## **EPIX PHARMACEUTICALS, INC.**

### **NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

#### ***Translation of Foreign Currencies***

The functional currency of the Company's foreign subsidiary is the U.S. dollar. The subsidiary's financial statements are remeasured into U.S. dollars using current rates of exchange for monetary assets and liabilities and historical rates of exchange for nonmonetary assets.

#### ***Cash Equivalents***

The Company considers investments with an original maturity of three months or less when purchased to be cash equivalents. Cash equivalents consist of money market accounts and commercial paper.

#### ***Marketable Securities***

The Company accounts for marketable securities in accordance with Statement of Financial Accounting Standards ("SFAS") No. 115, "*Accounting for Certain Investments in Debt and Equity Securities*" ("SFAS 115"). SFAS 115 establishes the accounting and reporting requirements for all debt securities and for investments in equity securities that have readily determinable fair values. Marketable securities consist of investment-grade corporate bonds, asset-backed debt securities and government-sponsored agency debt securities. The Company classifies its marketable securities as available-for-sale and, as such, carries the investments at fair value, with unrealized holding gains and losses included in accumulated other comprehensive income or loss. The cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion are included in interest income. Realized gains or losses and declines in value judged to be other-than-temporary on available-for-sale securities are included in interest income. The cost of securities is based on the specific identification method.

#### ***Fair Value of Financial Instruments***

At December 31, 2007, the Company's financial instruments consisted of cash and cash equivalents, available-for-sale marketable securities and debt. At December 31, 2006, the Company's financial instruments also included a derivative resulting from the merger consideration due to the former Predix option and shareholders. The carrying value of cash equivalents approximates fair value due to their short-term nature. The carrying value of the available-for-sale marketable securities and convertible debt is further discussed in Notes 3 and 8, respectively. The fair value of the 3.0% convertible senior notes, which is based on quoted market prices, was \$68.0 million at December 31, 2007.

At December 31, 2006, the Company had an embedded derivative resulting from the terms of the \$15.0 million milestone payment that was due to the former Predix optionholders and shareholders on October 29, 2007. Under the terms of the merger agreement, the former Predix optionholders were required to be paid in cash while the remainder of the Predix shareholders were required to be paid in shares to the extent allowable under the agreement. The number of shares to be issued was determined based on 75% of the 30-day average closing price of the Company's common stock on the NASDAQ Global Market ending on the trading day that was ten days prior to the payment date. The \$15.0 million milestone payment plus accrued interest was paid by the Company through the issuance of 3,167,000 of its common shares and \$5.8 million of cash. The value of this embedded derivative at December 31, 2006 was \$3.0 million and was recorded as part of the merger consideration payable on the accompanying balance sheet. The value of the derivative on the milestone payment date was \$2.2 million. Increases (decreases) in the value of the embedded derivative of \$(0.8) million and \$0.9 million during the years ended December 31, 2007 and 2006, respectively, were recorded in interest expense in the statement of operations.

## **EPIX PHARMACEUTICALS, INC.**

### **NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

#### ***Concentrations of Credit Risk***

Financial instruments that potentially subject the Company to concentrations of credit risk primarily consist of cash equivalents and available-for-sale marketable securities. In accordance with the Company's investment policy, marketable securities are principally restricted to U.S. government securities, high-grade bank obligations, high-grade corporate bonds, commercial paper, asset-backed securities and certain money market funds. Although the vast majority of the Company's \$61.1 million of cash, cash equivalents and available-for-sale marketable securities were invested through one investment advisor as of December 31, 2007, the credit risk exposure of its investments was limited because of a diversified portfolio that included asset-backed securities and commercial paper such as Morgan Stanley, American General Finance, General Electric and Unicredito Italiano; high-grade corporate bonds and money market funds.

#### ***Property and Equipment***

Property and equipment are recorded at historical cost. Depreciation on laboratory equipment, furniture and fixtures and other equipment is determined using the straight-line method over the estimated useful lives of the related assets, ranging from 2 to 5 years. Leasehold improvements are amortized using the straight-line method over the shorter of the asset life or the remaining life of the lease. Expenditures for maintenance and repairs are charged to expense as incurred; improvements which extend the life or use of equipment are capitalized.

#### ***Long-Lived Assets***

In accordance with SFAS No. 144, "*Accounting for the Impairment or Disposal of Long-Lived Assets*," the Company recognizes impairment losses on long-lived assets when indicators of impairment are present and future undiscounted cash flows are insufficient to support the assets' recovery.

#### ***Other Assets***

Included in other assets at December 31, 2007 is restricted cash in the amount of \$1.4 million. Restricted cash consists of amounts held in deposit at a financial institution to collateralize standby letters of credit in the name of the Company's landlords in accordance with certain facility lease agreements.

#### ***Goodwill***

The Company assesses the realizability of goodwill annually and whenever events or changes in circumstances indicate it may be impaired. The Company completed its annual test for impairment at July 1, 2007 and determined that goodwill was not impaired. No factors occurred subsequent to July 1, 2007 to evidence any impairment as of December 31, 2007.

#### ***Income Taxes***

The Company provides for income taxes under SFAS No. 109, "*Accounting for Income Taxes*." Under this method, deferred taxes are recognized using the liability method, whereby tax rates are applied to cumulative temporary differences between carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes and are based on when and how they are expected to affect the tax return. A valuation allowance is provided to the extent that there is uncertainty as to the Company's ability to generate sufficient taxable income in the future to realize the benefit from its net deferred tax asset.

## EPIX PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

#### *Segment Information*

SFAS No. 131, "Disclosure about Segments of an Enterprise and Related Information," establishes standards for reporting information regarding operating segments and for related disclosures about products and services and geographical areas. The Company operates in one business segment, which is the development of pharmaceutical products.

#### *Revenue*

For the years ended December 31, 2007 and 2006 GlaxoSmithKline represented 53% and 1%, respectively, of total revenues and Cystic Fibrosis Foundation Therapeutics, Incorporated represented 25% and 15%, respectively, of total revenues. There were no revenues from these two collaboration partners in 2005.

The Company recognizes revenue relating to collaborations in accordance with the SEC's Staff Accounting Bulletin ("SAB") No. 104, "Revenue Recognition in Financial Statements," ("SAB 104"). Revenue under collaborations may include the receipt of non-refundable license fees, milestone payments, research and development payments and royalties.

The Company recognizes nonrefundable upfront license fees and guaranteed, time-based payments that require continuing involvement in the form of research and development as revenue:

- ratably over the development period; or
- based upon the level of research services performed during the period of the research contract.

When the period of deferral cannot be specifically identified from the contract, the Company estimates the period based upon other critical factors contained within the contract. EPIX continually reviews such estimates which could result in a change in the deferral period and might impact the timing and amount of revenue recognized.

Milestone payments which represent a significant performance risk are recognized as product development revenue when the performance obligations, as defined in the contract, are achieved. Performance obligations typically consist of significant milestones in the development life cycle of the related technology, such as the filing of investigational new drug applications, initiation of clinical trials, filing for approval with regulatory agencies and approvals by regulatory agencies.

Reimbursements of research and development costs are recognized as product development revenue as the related costs are incurred.

Royalties are recognized as revenue when earned, are reasonably estimable and collection is probable, which is typically upon receipt of royalty reports from the licensee or cash.

#### *Product development revenue*

In June 2000, the Company entered into a strategic collaboration agreement with Bayer Schering Pharma AG, Germany, whereby each party to the agreement shares equally in Vasovist development costs and U.S. operating profits and the Company will receive royalties related to non-U.S. sales. The Company recognizes as revenue costs incurred by the Company in excess of the Company's obligation under the agreement to expend 50% of the costs to develop Vasovist. This revenue is recognized in the same period in which the costs are incurred. With respect to payments due to Bayer Schering Pharma AG, Germany, if any, in connection with the Vasovist development program, the Company recognizes such amounts as a reduction in revenue at the time Bayer Schering Pharma AG, Germany performs the research and development activities for which the Company is obligated to pay Bayer Schering Pharma AG, Germany.

## EPIX PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

On a quarterly basis, the Company calculates the revenue or reduction in revenue, as the case may be, with respect to the collaboration with Bayer Schering Pharma AG, Germany for Vasovist as follows:

- The Company calculates its development costs directly related to Vasovist.
- The Company obtains cost reports from Bayer Schering Pharma AG, Germany for costs incurred by Bayer Schering Pharma AG, Germany related to the development of Vasovist during the same period.
- The Company multiplies its and Bayer Schering Pharma AG, Germany's development costs by approximately 50% based on the contractual allocation of work contemplated under the agreement.
- The Company then records the net difference as development revenue if the balance results in a payment to the Company and negative revenue if the balance results in a payment to Bayer Schering Pharma AG, Germany.

The result of this calculation is that the Company records revenue only for amounts it is owed by Bayer Schering Pharma AG, Germany in excess of 50% of development expenses of the project in the particular period. The Company records a reduction in revenue for any amounts owed to Bayer Schering Pharma AG, Germany in the particular period.

The additional payments made by Bayer Schering Pharma AG, Germany to the Company represent revenue to the Company because the Company is providing additional services to Bayer Schering Pharma AG, Germany which Bayer Schering Pharma AG, Germany was contractually obligated to perform itself. For example, the Company performed substantial amounts of the work on behalf of Bayer Schering Pharma AG, Germany to prepare the regulatory submission to the European regulatory authorities for Vasovist which would otherwise have been Bayer Schering Pharma AG, Germany's responsibility under the agreement. Had the Company not performed these and other additional services, Bayer Schering Pharma AG, Germany would have had to contract with a third-party to perform the work or Bayer Schering Pharma AG, Germany would have had to perform the work itself.

In May 2003, the Company entered into a development agreement with Bayer Schering Pharma AG, Germany for EP-2104R and a collaboration agreement with Bayer Schering Pharma AG, Germany for MRI research. Under the EP-2104R development agreement, Bayer Schering Pharma AG, Germany agreed to make fixed payments totaling approximately \$9.0 million to the Company over a two year period, which began in the second quarter of 2003 and ended in the fourth quarter of 2004, to cover a portion of the Company's expenditures for the EP-2104R feasibility program. The Company recognized revenue from Bayer Schering Pharma AG, Germany for the feasibility program in proportion to actual cost incurred relative to the estimated total program costs. During the third quarter of 2006, the Company completed its work on the feasibility program. On July 13, 2006, Bayer Schering Pharma AG, Germany determined not to exercise its option for the development of EP-2104R. Under the terms of the agreement, EPIX will retain full rights to the EP-2104R program. Revenue under the MRI research collaboration was recognized at the time services were provided. The MRI research program was completed in the second quarter of 2006.

The Company is a party to collaboration agreements with GlaxoSmithKline and CFFT. Under the agreements, EPIX receives cost reimbursements and research funding and may earn milestone payments in accordance with the terms of the agreements. The reimbursements of research and development costs are being recognized as revenue as the related costs are incurred. As EPIX is the party responsible for providing the research services, EPIX is recognizing the reimbursement of the costs associated with EPIX's research efforts as revenue, not as a net research expense. EPIX recognizes milestone payments as revenue when the related performance obligation, as defined in the agreement, has been achieved.

Payments received by the Company from collaboration partners in advance of the Company performing research and development activities are recorded as liabilities on the balance sheet.

## EPIX PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

#### *Royalty revenue*

The Company receives a royalty on sales of Vasovist outside of the United States and on sales of Primovist by Bayer Schering Pharma AG, Germany. Commercial launch of Vasovist in the European Union began on a country-by-country basis in the second quarter of 2006. Vasovist has also received regulatory approval in Canada, Iceland, Turkey, Norway, Switzerland and Australia. The Company recognizes royalty revenue from sales of Vasovist and Primovist in the quarter when Bayer Schering Pharma AG reports those sales to the Company.

The Company also earned royalty revenue pursuant to its sub-license on certain of its patents to Bracco Imaging S.p.A. ("Bracco"). Due to the expiration of patents, the royalty revenue from Bracco ended in the second quarter of 2007.

#### *License fee revenue*

The Company records license fee revenue in accordance with SAB 104. Pursuant to SAB 104, the Company recognizes revenue from non-refundable license fees and milestone payments, not specifically tied to a separate earnings process, ratably over the period during which the Company has a substantial continuing obligation to perform services under the contract. When milestone payments are specifically tied to a separate earnings process, revenue is recognized when the specific performance obligations associated with the payment are completed.

In December 2006, the Company established a worldwide multi-target strategic collaboration with GlaxoSmithKline to discover, develop and market novel medicines targeting four G-protein coupled receptors (GPCRs) for the treatment of a variety of diseases, including EPIX's novel 5-HT<sub>4</sub> partial agonist program, PRX-03140, in early-stage clinical development for the treatment of Alzheimer's disease. EPIX received \$17.5 million of up front payments which is included in deferred revenue and will be recorded as revenue ratably from the time of payment until the expiration of the contract in December 2020.

In connection with the acquisition of Predix, the Company is recognizing license fee revenue for arrangements that Predix had with both Amgen and CFFT. The Company ascribed \$3.4 million and \$0.2 million of value to these arrangements, respectively, on the date of acquisition based upon the fair value of the remaining services to be provided by EPIX. The deferred revenue is being recognized ratably over the period in which the Company is required to provide services, which was October 2007 for Amgen and July 2009 for CFFT.

In September 2001, the Company sub-licensed certain patents to Bracco and received a \$2.0 million license fee from Bracco. This license fee was included in deferred revenue and was recorded as revenue ratably from the time of the payment until the expiration of MGH's patents, which occurred in the European Union in May 2006 and in the United States in November 2006.

As part of the Company's strategic collaboration agreement with Bayer Schering Pharma AG, Germany for Vasovist entered into in 2000, the Company granted Bayer Schering Pharma AG, Germany an exclusive license to co-develop and market Vasovist worldwide, exclusive of Japan. Later in 2000, the Company amended this strategic collaboration agreement to grant Bayer Schering Pharma AG, Germany exclusive rights to develop and market Vasovist in Japan. The Company received a \$3.0 million license fee from Bayer Schering Pharma AG, Germany in connection with that amendment. This license fee is included in deferred revenue. The Company is amortizing this revenue over the term of the contract and will continue to review this estimate and make appropriate adjustments as information becomes available.

Pursuant to an earlier collaboration agreement with Covidien Ltd. (formerly known as Tyco International Ltd.), the Company recorded \$4.4 million of deferred revenue. The Company is amortizing this revenue over

# EPIX PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

the term of the contract due to the uncertainty of the timing of approval in United States. The Company will continue to review this estimate and make appropriate adjustments as information becomes available.

### *Research and Development Expenses*

Research and development costs, including those associated with technology and licenses, are expensed as incurred. Research and development costs primarily include employee salaries and related costs, third-party service costs, the cost of preclinical and clinical trials, supplies, consulting expenses, facility costs and certain overhead costs.

In order to conduct research and development activities and compile regulatory submissions, the Company enters into contracts with vendors who render services over extended periods of time. Typically, the Company enters into three types of vendor contracts: time-based, patient-based or a combination thereof. Under a time-based contract, using critical factors contained within the contract, usually the stated duration of the contract and the timing of services provided, the Company records the contractual expense for each service provided under the contract ratably over the period during which the Company estimates the service will be performed. Under a patient-based contract, the Company first determines an appropriate per patient cost using critical factors contained within the contract, which include the estimated number of patients and the total dollar value of the contract. The Company then records expense based upon the total number of patients enrolled in the clinical study during the period. On a quarterly basis, the Company reviews the assumptions for each contract in order to reflect the Company's most current estimate of the costs incurred under each contract. Adjustments are recorded in the period in which the revisions are estimable. These adjustments could have a material effect on the Company's results of operations.

### *Loss Per Share*

The Company computes loss per share in accordance with the provisions of SFAS No. 128, "Earnings per Share." Basic net loss per share is based upon the weighted-average number of common shares outstanding and excludes the effect of dilutive common stock issuable upon exercise of stock options, convertible debt and merger consideration. In computing diluted loss per share, only potential common shares that are dilutive, or those that reduce earnings per share, are included. The issuance of common stock from the exercise of options, convertible debt and merger consideration is not assumed if the result is anti-dilutive, such as when a loss is reported.

Common stock potentially issuable but excluded from the calculation of dilutive net loss per share for the years ended December 31, 2007, 2006 and 2005 because their inclusion would have been antidilutive consisted of the following:

	<u>2007</u>	<u>2006</u>	<u>2005</u>
Stock options and awards .....	3,847,386	3,427,107	2,181,184
Shares issuable on conversion of 3% Convertible Senior Notes(A) .....	2,239,393	2,239,393	2,239,393
Shares issuable in satisfaction of merger consideration payable(B) .....	<u>—</u>	<u>3,008,726</u>	<u>—</u>
Total .....	<u>6,086,779</u>	<u>8,675,226</u>	<u>4,420,577</u>

- (A) Each \$1,000 of senior notes is convertible into 22.39 shares of the Company's common stock representing a conversion price of approximately \$44.66 per share if (1) the price of the Company's common stock trades above 120% of the conversion price for a specified time period, (2) the trading price of the senior notes is below a certain threshold, (3) the senior notes have been called for redemption, or (4) specified

## **EPIX PHARMACEUTICALS, INC.**

### **NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

corporate transactions have occurred. None of these conversion triggers have occurred as of December 31, 2007.

- (B) Share amount calculated as if the merger consideration was payable as of December 31, 2006. Actual settlement occurred on October 29, 2007 as the Company issued 3,167,000 shares of common stock and paid \$5.8 million in cash.

#### ***Comprehensive Loss***

In accordance with SFAS No. 130, "*Reporting Comprehensive Income*" components of comprehensive loss include net loss and certain transactions that have generally been reported in the statements of stockholders' equity (deficit). Other comprehensive loss is comprised of unrealized gains or losses on available-for-sale marketable securities.

#### ***Employee Stock Compensation***

The Company adopted the provisions of SFAS No. 123(R), "*Share-Based Payment — An Amendment of FASB Statements No. 123 and 95*" ("SFAS 123(R)"), beginning January 1, 2006, using the modified prospective transition method. Under the modified prospective transition method, financial statements for periods prior to the adoption date are not adjusted for the change in accounting. Compensation expense is now recognized, based on the requirements of SFAS 123(R), for (a) all share-based payments granted after the effective date and (b) all awards granted to employees prior to the effective date that remain unvested on the effective date.

Prior to adopting SFAS 123(R), the Company used the intrinsic value method to account for stock-based compensation under Accounting Principles Board Opinion No. 25, "*Accounting for Stock Issued to Employees*" ("APB 25"). As a result of the adoption of SFAS 123(R), the Company is amortizing the unamortized stock-based compensation expense related to unvested option grants issued prior to the adoption of SFAS 123(R). The Company has elected to continue to use the Black-Scholes option pricing model to determine the fair value of options. SFAS 123(R) also requires companies to utilize an estimated forfeiture rate when calculating the expense for the period, whereas SFAS 123 permitted companies to record forfeitures based on actual forfeitures, which was the Company's historical policy under the disclosure requirements of SFAS 123. As a result, the Company has applied an estimated forfeiture rate to remaining unvested awards based on historical experience in determining the expense recorded in the Company's consolidated statements of operations. This estimate is evaluated quarterly and the forfeiture rate will be adjusted as necessary. The actual expense recognized over the vesting period will only be for those shares that vest during that period. The Company has also elected to recognize compensation cost for awards with pro-rata vesting using the straight-line method.

#### ***Reclassifications***

Certain items in the prior year's consolidated financial statements have been reclassified to conform to the current presentation of the financial statements.

#### ***Recent Accounting Pronouncements***

On September 15, 2006, the FASB issued SFAS No. 157 "*Fair Value Measurements*." SFAS 157 defines fair value, establishes a framework for measuring fair value and expands disclosures about fair value measurements. SFAS 157 is effective for the Company as of January 1, 2008. The Company does not expect SFAS 157 will have a material impact on its financial condition or results of operations.

In February 2007, the FASB issued SFAS No. 159, "*The Fair Value Option for Financial Assets and Financial Liabilities — Including an Amendment of FASB Statement No. 115*," ("SFAS 159") which is effective for fiscal years beginning after November 15, 2007. SFAS 159 permits an entity to choose to measure many

# EPIX PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings. The Company does not expect SFAS 159 will have a material impact on its financial condition or results of operations.

In June 2007, the FASB reached a consensus on EITF Issue No. 07-03, "Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities." EITF 07-03 requires companies to defer and capitalize, until the goods have been delivered or the related services have been rendered, non-refundable advance payments for goods that will be used or services that will be performed in future research and development activities. EITF 07-03 is effective for fiscal years beginning after December 15, 2007. The Company does not expect EITF 07-03 will have a material impact on its financial condition or results of operations.

In December 2007, the FASB issued SFAS No. 141(R), "Business Combinations." This Statement provides greater consistency in the accounting and financial reporting of business combinations. It requires the acquiring entity in a business combination to recognize all assets acquired and liabilities assumed in the transaction, establishes the acquisition-date fair value as the measurement objective for all assets acquired and liabilities assumed, and requires the acquirer to disclose the nature and financial effect of the business combination. FAS 141(R) is effective for fiscal years beginning after December 15, 2008. The Company is currently assessing the impact the adoption will have on the Company's financial position and results of operations.

### 3. Marketable Securities

The estimated fair value of marketable securities is determined based on broker quotes or quoted market prices or rates for the same or similar instruments. The estimated fair value and cost of marketable securities are as follows at December 31:

	2007		2006	
	Fair Value	Cost	Fair Value	Cost
Government-sponsored agency securities . . . . .	\$ —	\$ —	\$61,036,088	\$61,002,190
Corporate bonds . . . . .	2,565,474	2,566,837	16,348,698	16,342,795
Commercial paper . . . . .	35,357,829	35,206,400	1,825,644	1,828,137
Asset backed securities . . . . .	13,524,757	13,511,763	—	—
Certificates of deposit . . . . .	471,068	471,068	—	—
	<u>\$51,919,128</u>	<u>\$51,756,068</u>	<u>\$79,210,430</u>	<u>\$79,173,122</u>

All of the Company's marketable securities as of December 31, 2007 and 2006 are classified as available-for-sale and by contractual maturity are due within one year.

Gross unrealized gains on marketable securities amounted to \$164,423 and \$41,980 in 2007 and 2006, respectively. Gross unrealized losses on marketable securities amounted to \$1,363 and \$4,672 in 2007 and 2006, respectively. The aggregate fair value of investments with unrealized losses was \$2.5 million and \$15.0 million at December 31, 2007 and 2006, respectively. All such investments have been in an unrealized loss position for less than one year. There were no realized gains or losses on marketable securities in 2007, 2006 and 2005.

### 4. Acquisition of Predix

On August 16, 2006, EPIX completed its acquisition of Predix pursuant to the terms of the merger agreement, whereby Predix merged with and into EPIX Delaware, Inc. and became a wholly-owned subsidiary

# EPIX PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

of EPIX. The merger with Predix was primarily a stock transaction valued at approximately \$125.0 million, including the assumption of net debt at closing. As part of the merger, the Company also assumed all outstanding options and warrants to purchase capital stock of Predix. The purchase price included a milestone payment of \$35.0 million in cash, stock or a combination of both based on Predix having achieved a strategic milestone under the merger agreement. Pursuant to the terms of the merger agreement, the Company paid \$20.0 million of the milestone payment in cash on October 29, 2006. The remaining \$15.0 million of the milestone payment plus accrued interest was paid on October 29, 2007 through the issuance of 3,167,000 of common shares and \$5.8 million in cash. The results of Predix have been included in the statements of operations from August 16, 2006.

The following unaudited pro forma financial information presents the results of operations as if the merger had occurred at the beginning of 2006. The 2006 period excludes the write-off of in-process research and development of \$123.5 million as it has no continuing impact after the merger. The pro forma information does not purport to indicate the results that would have actually been obtained had the merger been completed on the assumed date or which may be realized in the future. Amounts in thousands, except per share data.

	Year Ended December 31, 2006
Revenues . . . . .	\$ 10,865
Net loss . . . . .	\$(57,592)
Net loss per share, basic and diluted . . . . .	\$ (1.79)

### 5. Property and Equipment

Property and equipment consist of the following:

	December 31,	
	2007	2006
Leasehold improvements . . . . .	\$ 3,766,584	\$ 4,444,244
Laboratory equipment . . . . .	2,777,731	2,524,697
Furniture, fixtures and other equipment . . . . .	3,020,935	2,164,636
	9,565,250	9,133,577
Less accumulated depreciation and amortization . . . . .	(3,520,364)	(5,541,007)
	<u>\$ 6,044,886</u>	<u>\$ 3,592,570</u>

### 6. Accrued Expenses

Accrued expenses consist of the following:

	December 31,	
	2007	2006
Accrued contractual product development expenses . . . . .	\$3,407,600	\$2,021,998
Accrued compensation . . . . .	2,184,368	1,968,127
Other accrued expenses . . . . .	2,507,571	3,705,423
	<u>\$8,099,539</u>	<u>\$7,695,548</u>

### 7. Restructuring Charges

During the second quarter of 2007, the Company incurred a restructuring charge of \$0.5 million for the consolidation of its leased laboratory facility in Cambridge, Massachusetts into the Company's Lexington,

**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

Massachusetts facility. The charge consisted primarily of future lease costs through the end of 2007. The consolidation was completed during the second quarter of 2007. In addition, during the second quarter of 2007, the Company recorded a reduction of its 2006 restructuring charge in the amount of \$0.1 million relating to a reduction in the amount of square footage leased at the Company's former headquarters location in Cambridge, Massachusetts.

Restructuring costs of \$1.0 million incurred in 2005 related to severance and related benefits for actions taken by management to control costs and improve the focus of operations in order to reduce losses and conserve cash. The Company reduced its workforce by 48 employees, or approximately 50%, in response to the FDA's second approvable letter regarding Vasovist. The reductions, which were completed in January 2006, affected both the research and development and the general and administrative areas of the Company. The 2006 costs included approximately \$0.4 million related to the 2005 restructuring plan for additional severance costs as well as costs related to vacating certain leased space and the write-off of leasehold improvements. In addition, in the third quarter of 2006, the Company recorded additional restructuring charges of \$0.2 million for facility exit costs related to the consolidation of the Company's Cambridge, MA headquarters into the former Predix headquarters in Lexington, MA. These costs primarily consist of future lease payments through the end of 2007 and the write off of leasehold improvements.

The following table displays the restructuring activity and liability balances:

	<u>Severance</u>	<u>Asset Write Off</u>	<u>Lease Obligation</u>	<u>Total</u>
Restructuring charges in fourth quarter of 2005 .....	\$ 971,828	\$ —	\$ —	\$ 971,828
Balance at December 31, 2005 .....	971,828	—	—	971,828
Restructuring charge .....	134,642	177,906	320,690	633,238
Cash payments .....	(1,106,470)	—	(90,714)	(1,197,184)
Non-cash items .....	—	(177,906)	—	(177,906)
Balance at December 31, 2006 .....	—	—	229,976	229,976
Restructuring charge .....	—	—	482,535	482,535
Cash payments .....	—	—	(580,113)	(580,113)
Reduction of 2006 restructuring charge .....	—	—	(132,398)	(132,398)
Balance at December 31, 2007 .....	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ —</u>

**8. Financing Arrangements**

***Convertible Debt***

In June 2004, the Company completed a sale, pursuant to Rule 144A under the Securities Act of 1933, of \$100.0 million of 3% convertible senior notes due 2024 for net proceeds of approximately \$96.4 million. Each \$1,000 of senior notes is convertible into 22.39 shares of the Company's common stock representing a conversion price of approximately \$44.66 per share if (1) the price of the Company's common stock trades above 120% of the conversion price for a specified time period, (2) the trading price of the senior notes is below a certain threshold, (3) the senior notes have been called for redemption, or (4) specified corporate transactions have occurred. None of these conversion triggers has occurred as of December 31, 2007. Each of the senior notes is also convertible into the Company's common stock in certain other circumstances. The senior notes bear an interest rate of 3%, payable semiannually on June 15 and December 15. Interest payments of \$3.0 million were made during each of the years ended December 31, 2007, 2006 and 2005. The senior notes are unsecured.

## EPIX PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

The Company has the right to redeem the notes on or after June 15, 2009 at an initial redemption price of 100.85%, plus accrued and unpaid interest. Noteholders may require the Company to repurchase the notes at par, plus accrued and unpaid interest, on June 15, 2011, 2014 and 2019 and upon certain other events, including a change of control and termination of trading of the Company's common stock on the NASDAQ Global Market.

In connection with the issuance of the senior notes, the Company incurred \$3.65 million of issuance costs, which primarily consisted of investment banker fees and legal and other professional fees. The costs are being amortized as interest expense using the effective interest method over the term from issuance through the first date that the holders are entitled to require repurchase of the senior notes (June 2011). For the years ended December 31, 2007, 2006 and 2005, amortization of the issuance costs was \$510,184, \$492,337 and \$475,115 respectively.

#### *Loan Agreement to Strategic Partner*

In May 2003, the Company entered into a Non-Negotiable Note and Security Agreement (the "Loan Agreement") with Bayer Schering Pharma AG, Germany under which the Company was eligible to borrow up to a total of \$15.0 million. The Loan Agreement carried a variable, market-based interest rate. In January 2006, the Company and Bayer Schering Pharma AG, Germany agreed to terminate the Loan Agreement.

#### **9. Commitments and Contingencies**

##### *Leases*

The Company leases facilities in Lexington, MA, Princeton, NJ and facilities and vehicles in Ramat Gan, Israel under agreements that are accounted for as operating leases. On August 31, 2006, the Company entered into an amended lease agreement for its Lexington facility, which expanded the space under lease from approximately 29,000 square feet to approximately 57,000 square feet. The Company's facility leases generally provide for a base rent plus real estate taxes and certain operating expenses related to the leases. Certain of the Company's leases contain renewal options, escalating payments over the life of the lease and landlord allowances. Scheduled rent increases and landlord allowances are being amortized over the terms of the agreements using the straight-line method, and are included in other liabilities in the accompanying consolidated balance sheet. The Company leases certain equipment under capital lease agreements. The Company has assets under capital lease obligations amounting to \$593,138 as of December 31, 2007. Amortization of such equipment is included in depreciation expense.

# EPIX PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

At December 31, 2007, future minimum commitments under all noncancellable capital and operating leases with initial or remaining terms of more than one year are as follows:

	Capital Leases	Operating Leases
2008 .....	\$ 208,478	\$ 2,698,410
2009 .....	139,163	2,546,501
2010 .....	58,848	2,489,469
2011 .....	—	2,127,495
2012 .....	—	1,725,868
Thereafter .....	—	3,792,517
Total minimum lease payments .....	406,489	15,380,260
Less aggregate future sublease income .....	—	(1,960,466)
	406,489	<u>\$13,419,794</u>
Less amount representing interest .....	(43,882)	
Present value of minimum lease payment .....	362,607	
Less current portion of capital lease obligation .....	(179,859)	
Capital lease obligations, net of current portion .....	<u>\$ 182,748</u>	

The Company has subleased its leased facility in Princeton, NJ. Total rental expense amounted to \$3.1 million, \$1.5 million and \$1.3 million for the years ended December 31, 2007, 2006 and 2005, respectively.

### Other Commitments

In November 2003, the Company entered into an intellectual property agreement with Martin R. Prince M.D., Ph.D. (the "Prince Agreement"). Under the terms of the Prince Agreement, Dr. Prince granted the Company certain discharges, licenses and releases in connection with the historic and future use of Vasovist by the Company and agreed not to sue the Company for intellectual property infringement related to the use of Vasovist. In consideration for Dr. Prince entering into this agreement, the Company paid him an upfront fee of \$850,000, issued him 88,000 shares of common stock valued at \$2.3 million (at the date of the agreement), agreed to pay him future royalties on sales of Vasovist and agreed to provide him with \$140,000 worth of Vasovist annually for the life of the agreement. The Company recorded a \$3.2 million charge to research and development expense in the fourth quarter of 2003 for the value of the cash and common stock consideration paid to Dr. Prince. During the third quarter of 2006, the obligation to provide Dr. Prince with \$140,000 of Vasovist annually was triggered and the Company recorded a \$0.9 million charge to research and development expense representing the present value of this obligation. Under the terms of the Prince Agreement, Dr. Prince may decide to defer delivery of all or a portion of the amount of Vasovist due to him in any given year to future years. The Prince Agreement expires based upon the last to expire patent or patent application as listed in the agreement, which is currently estimated to be in 2026. As of December 31, 2007 no Vasovist product had been requested by or provided to Dr. Prince.

### Informal SEC Investigation

On December 8, 2006, the Company created a special board committee of independent directors to conduct a review of the Company's historical stock option practices. The special committee completed its investigation and concluded that certain employees, including certain members of the Company's former senior management, prior to the change in the Company's senior management in connection with the merger with

## EPIX PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

Predix in August 2006, had retrospectively selected dates for the grant of certain stock options and re-priced, as defined by financial accounting standards, certain options during the period from 1997 through 2005. As a result, in connection with the filing of the Company's 2006 Form 10-K, the Company restated its financial statements to record additional non-cash stock-based compensation expense and related payroll tax effects, with regard to these past stock option grants. The SEC is conducting an informal inquiry into the Company's stock option grants and practices and related accounting. The Company's past stock option practices and the restatement of its prior financial statements expose the Company to greater risks associated with litigation, regulatory, or other proceedings, as a result of which the Company could be required to pay significant fines or penalties.

#### 10. Stockholders' Equity

##### *Common Stock*

In December 2006, the Company filed a shelf registration statement on Form S-3 with the Securities and Exchange Commission to allow the Company to issue, in one or more offerings, up to \$75 million in common stock, preferred stock or warrants. Due to the Company not filing its 2006 Annual Report on Form 10-K timely, any take downs on this shelf registration statement are prohibited until such time that the Company has timely filed its quarterly and annual reports for a consecutive 12-month period following the missed filing (ending in April 2008) and the Company has met the other requirements of Form S-3 at the time it files its Annual Report on Form 10-K for fiscal 2007. All filings subsequent to the 2006 Annual Report on Form 10-K have been timely filed.

In conjunction with the Company entering into a collaboration agreement with GlaxoSmithKline on December 11, 2006, the Company entered into a stock purchase agreement with GlaxoSmithKline. Pursuant to this agreement, GlaxoSmithKline purchased 3,009,027 shares of the Company's common stock for \$17,500,000.

On November 9, 2007, the Company entered into Securities Purchase Agreements pursuant to which it sold in a private placement to institutional and accredited investors an aggregate of 5,245,468 shares of the Company's common stock, \$0.01 par value per share, at a per share purchase price of \$3.10, which represented a discount of approximately 15% to the closing bid price of the Common Stock as reported on the NASDAQ Global Market on November 8, 2007. Aggregate proceeds from the private placement, after deducting offering expenses, were approximately \$15.0 million. The closing of the private placement occurred on November 15, 2007. These shares were registered on Form S-1 in December 2007.

##### *Equity Plans*

The Company has in place an Amended and Restated 1992 Incentive Plan (the "Equity Plan"), which provides stock awards to purchase shares of common stock to be granted to employees and consultants. In June 2005, the Company amended the Equity Plan to increase the number of shares reserved for issuance pursuant to future grants by 333,333. The Equity Plan provides for the grant of stock options (incentive and non-statutory), stock appreciation rights, performance shares, restricted stock or stock units, for the purchase of an aggregate of 4,733,266 shares of common stock since the Equity Plan inception, subject to adjustment for stock-splits and similar capital changes. Awards under the Equity Plan may be granted to officers, employees and other individuals as determined by the compensation committee. The compensation committee also selects the participants and establishes the terms and conditions of each option or other equity right granted under the Equity Plan, including the exercise price, the number of shares subject to options or other equity rights and the time at which such options become exercisable. The stock options have a contractual term of ten years and generally vest over a period of four or five years. As of December 31, 2007, 617,414 shares of common stock are available for grant under the Equity Plan.

**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

The Company has in place an Amended and Restated 1996 Director Stock Option Plan (the "Director Plan"). All of the directors who are not employees of the Company are currently eligible to participate in the Director Plan. The number of shares underlying the option granted to each eligible director upon election or re-election is 25,000 shares. Each option becomes exercisable with respect to 8,334 shares on each anniversary date of grant for a period of three years, provided that the option holder is still a director of the Company at the opening of business on such date. In addition, each eligible director is automatically granted an option to purchase 10,000 shares annually during the years in which such director is not up for reelection. Such options become exercisable in full on the first anniversary date of the grant, provided the option holder is still a director of the Company at the opening of business on such date. The term of each option granted under the Director Plan is ten years from the date of grant. The exercise price for the options is equal to the fair value of the underlying shares at the date of grant. As of December 31, 2007, 48,670 shares of common stock are available for grant under the Director Plan.

In conjunction with the merger with Predix, the Company assumed the Predix Pharmaceuticals Holdings, Inc. Amended and Restated 2003 Stock Incentive Plan (the "2003 Plan"). The 2003 Plan provides for the grant of stock options (incentive and non-statutory), restricted stock and other stock awards having such terms and conditions as the board may determine. Under the 2003 Plan, stock awards may be granted to employees and to consultants of the Company. The options may be granted at a price not less than fair value of the common stock on the date of grant. At December 31, 2007, 922,113 shares of common stock were available for grant under the 2003 Plan. The Company assumed options to purchase 1,891,721 shares of Predix common stock as part of the merger. The value of the unvested portion of the options assumed amounted to \$5.4 million and is being recognized as compensation expense over the remaining vesting term of the options.

The Company has recorded \$4.8 million and \$4.2 million of stock-based compensation expense, which includes a charge for the shares issued under the Company's Employee Stock Purchase Plan (the "ESPP"), for the years ended December 31, 2007 and 2006, respectively. The stock-based compensation expense included \$2.5 million and \$2.7 million in research and development and \$2.3 million and \$1.5 million in general and administrative expense for the years ended December 31, 2007 and 2006, respectively. The compensation expense increased both basic and diluted net loss per share for the years ended December 31, 2007 and 2006 by \$0.14 and \$0.20, respectively. As of December 31, 2007, there was \$9.8 million of unrecognized compensation expense related to non-vested awards that is expected to be recognized over a weighted average period of 1.4 years.

The following table illustrates the effect on net loss and net loss per share for the year ended December 31, 2005 as if the Company had applied the fair value provisions of SFAS 123 to options granted under the Company's stock option plans.

Net loss — as reported .....	\$(21,268,958)
Add: employee stock-based compensation included in net loss .....	(3,021,815)
Deduct: pro forma adjustment for stock-based compensation .....	<u>(4,511,982)</u>
Net loss — pro forma .....	<u><u>\$(28,802,755)</u></u>
Net loss per share, basic and diluted	
As reported. ....	<u>\$ (1.37)</u>
Pro forma .....	<u><u>(1.86)</u></u>

The fair value of each stock option is estimated on the date of grant using the Black-Scholes option pricing model using the assumptions noted in the following table. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected life of the stock options. Expected volatility is based on historical volatility data of the Company's stock and comparable companies to the expected option

**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

term. The Company uses the "simplified" method, as prescribed by the SEC's SAB No. 107, to calculate the expected term, or life, of these options.

	Options			ESPP		
	Year Ended December 31,					
	2007	2006	2005	2007	2006	2005
Expected life of option (years) . . . . .	6.3	6.3	6.9	0.5	0.5	0.5
Expected stock price volatility . . . . .	70%	70%	83%	48%	71%	82%
Weighted average risk-free interest rate . . . . .	4.52%	4.69%	3.77%	4.30%	4.93%	3.51%
Expected annual dividend per share . . . . .	\$ —	\$ —	\$ —	\$ —	\$ —	\$ —

The weighted-average grant date fair value of stock options granted during 2007, 2006 and 2005 was \$3.69, \$4.54 and \$8.34 per share, respectively. The total intrinsic value of options exercised during 2007, 2006 and 2005 was \$1.6 million, \$1.8 million and \$0.2 million respectively.

A summary of option activity as of December 31, 2007 and changes during the year then ended is presented below:

	Shares	Weighted - Average Exercise Price	Weighted - Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2006. . . . .	3,427,107	\$7.14		
Granted . . . . .	1,414,587	5.58		
Exercised . . . . .	(361,154)	1.16		
Cancelled . . . . .	(633,154)	8.83		
Outstanding at December 31, 2007. . . . .	<u>3,847,386</u>	<u>\$6.85</u>	<u>7.85</u>	<u>\$2,543,267</u>
Exercisable at December 31, 2007 . . . . .	<u>1,596,565</u>	<u>\$7.65</u>	<u>6.76</u>	<u>\$1,900,294</u>
Vested and expected to vest at December 31, 2007 . . . . .	<u>3,519,088</u>	<u>\$6.91</u>	<u>7.75</u>	<u>\$2,489,443</u>

**2006 Employee Stock Purchase Plan**

The Company sponsors the 2006 Employee Stock Purchase Plan (the "Purchase Plan") under which employees may purchase shares of common stock at a discount from fair market value at specified dates. Employees purchased 54,731 shares in 2007 at an average price of \$3.72 per share. At December 31, 2007, 145,269 common shares remained available for issuance under the Purchase Plan. The Purchase Plan is intended to qualify as an employee stock purchase plan within the meaning of Section 423 of the Internal Revenue Code of 1986, as amended (the "Code"). Rights to purchase common stock under the Purchase Plan are granted at the discretion of the compensation committee, which determines the frequency and duration of individual offerings under the Purchase Plan and the dates when stock may be purchased. Eligible employees participate voluntarily and may withdraw from any offering at any time before stock is purchased. Participation terminates automatically upon termination of employment. The purchase price per share of common stock in an offering is 85% of the lesser of its fair market value at the beginning of the offering period or on the applicable exercise date and is paid through payroll deductions.

**EPIX PHARMACEUTICALS, INC.**

**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

**11. Income Taxes**

The Company has reported losses since inception and, due to the degree of uncertainty related to the ultimate use of the net operating loss carryforwards, has fully reserved this tax benefit. The Company has the following deferred tax assets as of December 31, 2007 and 2006:

	December 31,	
	2007	2006
Deferred tax assets:		
Net operating loss carry forwards . . . . .	\$ 65,651,000	\$ 48,269,000
Research and development tax credits . . . . .	1,274,000	857,000
Book over tax depreciation and amortization . . . . .	3,973,000	4,090,000
Deferred revenue . . . . .	6,301,000	7,323,000
Other . . . . .	1,536,000	1,487,000
Total deferred tax assets . . . . .	78,735,000	62,026,000
Valuation allowance . . . . .	(78,735,000)	(62,026,000)
Deferred income taxes, net . . . . .	\$ —	\$ —

As of December 31, 2007, the Company had approximately \$176.3 million of domestic NOL carry forwards and \$5.5 million of foreign NOL carryforwards, which either expire on various dates through 2028 or can be carried forward indefinitely. These loss carry forwards are available to reduce future federal, state and foreign taxable income, if any. As a result of ownership changes resulting from sales of equity securities, the Company's ability to use the net operating loss carry forwards is subject to annual limitations as defined in section 382 and 383 of the Code. The Company currently estimates that the annual limitation of its net operating losses generated through August 15, 2006 will be approximately \$8.5 million through 2011 and approximately \$2.4 million thereafter. The Company also estimates that the annual limitation on its use of acquired net operating losses generated through August 15, 2006 will be approximately \$6.5 million through 2010 and none thereafter. The Company is also eligible for research and development tax credits, which can be carried forward to offset federal taxable income. The annual limitation and the timing of attaining profitability may result in the expiration of net operating loss and tax credit carry forwards before utilization.

The valuation allowance relates to U.S. NOLs and deferred tax assets and certain other foreign deferred tax assets and is recorded based upon the uncertainty surrounding their realizability, as these assets can only be realized via profitable operations in the respective tax jurisdictions.

In accordance with SFAS No. 109, the accounting for tax benefits of acquired deductible temporary differences and NOL carry forwards, which are not recognized at the acquisition date because a valuation allowance is established and which are recognized subsequent to acquisitions, will be applied first to reduce to zero any goodwill and other non-current intangible assets related to the acquisitions. Any remaining benefits would be recognized as a reduction of income tax expense. As of December 31, 2007, \$16.0 million of the Company's deferred tax asset pertains to acquired companies, the future benefits of which will be applied first to reduce to zero any goodwill and other non-current intangible assets related to the acquisitions, prior to reducing income tax expense. Upon adoption of SFAS No. 141-R, "*Business Combinations*," the reduction of a valuation allowance that pertains to the acquired companies is generally recorded to reduce the Company's income tax expense.

# EPIX PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

The reconciliation of income tax computed at the U.S. federal statutory rate to income tax expense is as follows:

	Years Ended December 31,			Years Ended December 31,		
	2007	2006	2005	2007	2006	2005
Tax at U.S. statutory rate . . . . .	\$(21,328,352)	\$(53,464,281)	\$(7,217,169)	(34.00)%	(34.00)%	(34.00)%
Permanent differences, net of federal benefit . . . . .	832,198	43,305,862	18,185	1.33%	27.54%	0.09%
Foreign taxes . . . . .	58,118	145,313	41,991	0.09%	0.09%	0.20%
Operating losses not benefited . . .	<u>20,496,154</u>	<u>10,158,419</u>	<u>7,198,984</u>	<u>32.67%</u>	<u>6.46%</u>	<u>33.91%</u>
Income tax expense . . . . .	<u>\$ 58,118</u>	<u>\$ 145,313</u>	<u>\$ 41,991</u>	<u>0.09%</u>	<u>0.09%</u>	<u>0.20%</u>

The Company adopted Financial Interpretation Number 48, "Accounting for Uncertain Tax Positions" on January 1, 2007. FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements in accordance with FASB Statement No. 109, "Accounting for Income Taxes." FIN 48 prescribes a recognition threshold and measurement of a tax position taken or expected to be taken in a tax return. The Company did not establish any reserves for uncertain tax liabilities upon adoption of FIN 48 and has no reserves for uncertain tax positions as of December 31, 2007. The Company will account for interest and penalties related to uncertain tax positions as part of its provision for federal and state income taxes.

The Company is currently open to audit under the statute of limitations by the Internal Revenue Service, state, and foreign jurisdictions for various years from the Company's inception through 2007.

### 12. Defined Contribution Plan

The Company offers a defined contribution 401(k) plan, which covers substantially all US employees. The plan permits participants to make contributions from 1% to 15% of their compensation. The Company matches up to 3% of employees' contributions. During 2007, 2006 and 2005, the Company's match amounted to \$209,704, \$170,499, and \$243,486, respectively.

### 13. Strategic Alliances and Collaborations

The Company's business strategy includes entering into alliances with companies primarily in the pharmaceutical industry to facilitate the development, manufacture, marketing, sale and distribution of EPIX products.

#### *GlaxoSmithKline*

On December 11, 2006, the Company entered into a development and license agreement with SmithKline Beecham Corporation, doing business as GlaxoSmithKline, and Glaxo Group Limited to develop and commercialize medicines targeting four G-protein coupled receptors, or GPCRs, for the treatment of a variety of diseases, including an option to license the Company's 5-HT4 partial agonist, PRX-03140, and other medicines arising from the four research programs. The other three GPCR targets are new discovery programs. GlaxoSmithKline does not have options to any of the Company's other clinical programs besides PRX-03140. The collaboration with GlaxoSmithKline is being conducted through its Center of Excellence of External Drug Discovery.

Pursuant to the collaboration agreement, the Company granted GlaxoSmithKline an exclusive option to obtain exclusive, worldwide license rights to complete the development and to commercialize the products initially developed under each of the Company's four research programs under the collaboration agreement. In return for those options and in consideration of the development work to be performed by the Company under the collaboration agreement, GlaxoSmithKline paid the Company an initial payment of \$17.5 million. As part

## EPIX PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

of the collaboration, on December 11, 2006 the Company entered into a stock purchase agreement with GlaxoSmithKline providing for the issuance and sale to GlaxoSmithKline of 3,009,027 shares of the Company's common stock for an aggregate purchase price of \$17.5 million. In addition, the Company may be eligible for up to an aggregate of \$1.2 billion in additional nonrefundable option fees and milestone payments that relate to the achievement of certain development, regulatory and commercial milestones across the four research programs. The Company is also eligible to receive tiered, double-digit royalties based on net sales by GlaxoSmithKline of any products developed under the collaboration agreement. The specific royalty rates will vary depending upon a number of factors, including the total annual net sales of the product and whether it is covered by one of the Company's patents. GlaxoSmithKline's royalty obligation under the collaboration agreement generally terminates on a product-by-product and country-by-country basis upon the later of (i) the expiration of the Company's last patent claiming the manufacture, use, sale or importation of the product in the relevant country and (ii) twelve years after the first commercial sale of the product in the relevant country.

If GlaxoSmithKline does not exercise any of the four options, the collaboration agreement will expire upon the expiration of the last such option. Otherwise, the collaboration agreement will expire on a product-by-product and country-by-country basis upon the expiration of the royalty payment obligations for each product in each country.

Under the collaboration agreement, the Company has agreed to design, discover and develop, at its own cost, small molecule drug candidates targeting one of the four GPCRs on which the research programs are focused. The design, discovery and development efforts will be guided by a joint steering committee formed pursuant to the collaboration agreement. The first program is focused on the 5-HT<sub>4</sub> receptor and will include the Company's 5-HT<sub>4</sub> partial agonist drug candidate, PRX-03140, which is currently in early-stage clinical development for the treatment of Alzheimer's disease. The Company has retained an option to co-promote products successfully developed from the 5-HT<sub>4</sub> program in the United States. Under any such co-promotion arrangement, the collaboration agreement provides for GlaxoSmithKline to direct the promotional strategy and compensate the Company for its efforts in co-promoting the product.

The Company has responsibility and control for filing, prosecution or maintenance of any of its patents that are the subject of an option to GlaxoSmithKline under the collaboration agreement, provided that in the event an option is exercised, responsibility and control of the patents subject to such option transfers to GlaxoSmithKline.

The parties each have the right to terminate the collaboration agreement if the other party becomes insolvent or commits an uncured material breach of the collaboration agreement. In addition, GlaxoSmithKline has the right to terminate the collaboration agreement in its entirety, and to terminate its rights to any program developed under the collaboration agreement on a regional or worldwide basis, in each case without cause. Upon a termination of the collaboration agreement, depending upon the circumstances, the parties have varying rights and obligations with respect to the grant of continuing license rights, continued commercialization rights and continuing royalty obligations.

#### ***Amgen***

As part of the Predix merger, the Company assumed an obligation for an exclusive license agreement with Amgen Inc., entered into on July 31, 2006, to develop and commercialize products based on its preclinical compounds that modulate the S1P<sub>1</sub> receptor and compounds and products that may be identified by or acquired by Amgen and that modulate the S1P<sub>1</sub> receptor. The S1P<sub>1</sub> receptor is a cell surface GPCR found on white blood cells and in other tissues that is associated with certain autoimmune diseases, such as rheumatoid arthritis and multiple sclerosis.

Pursuant to the license agreement, the Company granted Amgen an exclusive worldwide license to its intellectual property and know-how related to the compounds in the Company's S1P<sub>1</sub> program that modulate

## EPIX PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

the S1P1 receptor, for the development and commercialization of those compounds and other compounds and products that modulate the S1P1 receptor. Amgen has limited rights to sublicense its rights under the license. In return for the license, Amgen paid the Company a nonrefundable, up-front payment of \$20.0 million and will pay royalties based on aggregate annual net sales of all S1P1-receptor-modulating products developed by Amgen under the license agreement. In addition, the Company may be eligible for up to an aggregate of \$287.5 million of nonrefundable milestone payments that relate to milestones associated with the commencement of clinical trials, regulatory approvals and annual net sales thresholds of the products under the license agreement. These royalty rates and milestone amounts are subject to reduction in the event that, among other things:

- Amgen is required to obtain third-party rights to develop and commercialize a product that incorporates an EPIX compound; and
- Amgen develops and commercializes products that are not covered by the intellectual property rights the Company licensed to Amgen, such as for example, S1P1-modulating products that may be acquired by Amgen from a third-party.

Generally, Amgen's royalty obligation under the agreement terminates on a product-by-product and country-by-country basis upon the later of (a) the expiration or termination of the last claim within the patents (whether such patents are patents EPIX licensed to Amgen or are patents owned or in-licensed by Amgen) covering such product and (b) ten years following the first commercial sale of the product. The agreement expires when all of Amgen's royalty obligations have terminated.

The Company has the option to co-promote one product from the collaboration in the United States for one indication to be jointly selected by EPIX and Amgen. During the first 15 months of the agreement, the Company was required to design, discover and develop, at its own cost, additional compounds that modulate the S1P1 receptor and that are within the same family of compounds as those identified in its patent applications licensed to Amgen under the agreement. The collaboration agreement provides Amgen with a license to these additional compounds to further its development efforts. The Company may undertake additional research under the agreement, at its own expense, as approved by a joint steering committee formed pursuant to the agreement. The Company has responsibility and control for filing, prosecution or maintenance for any of its patents licensed to Amgen for 24 months or until the start of Phase 1 clinical trials for the first product developed under the agreement, at which time, responsibility and control of such patents transfers to Amgen. Amgen has responsibility and control for filing, prosecution or maintenance for all other patents covered by the agreement, including patents jointly developed under the agreement. Amgen will have final decision making authority on all other research matters and will be responsible for non-clinical and clinical development, manufacturing, regulatory activities and commercialization of the compounds and products developed under the license agreement, at its own expense.

The parties each have the right to terminate the agreement (in whole or for specified products or countries, depending upon the circumstances) upon a material uncured breach by the other party and Amgen has the right to terminate the agreement for convenience upon varying periods of at least three months advance notice. Upon a termination of the agreement, depending upon the circumstances, the parties have varying rights and obligations with respect to the grant of continuing license rights, continued commercialization rights and continuing royalty obligations.

#### *Cystic Fibrosis Foundation Therapeutics, Incorporated*

In March 2005, Predix entered into a research, development and commercialization agreement with Cystic Fibrosis Foundation Therapeutics, Incorporated, or CFFT, the drug discovery and development affiliate of the Cystic Fibrosis Foundation. In August 2006, the Company expanded the research, development and commercialization agreement with CFFT. In November 2007, the Company and CFFT amended the agreement to

## EPIX PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

provide for approximately \$1.1 million of research funding for the CFTR program (as described below) until the parties negotiate a follow-on agreement for the further discovery and development of the CFTR program.

The CFFT agreement provides research funding for two discovery programs as described below.

- The first program is focused on correcting a malfunction of the Cystic Fibrosis Transmembrane conductance Regulator, or CFTR, ion channel protein. The Company is using its proprietary structure-based technologies to model the structure of this ion channel protein target and identify binding sites in the channel for therapeutic intervention. Once these sites are identified, the Company aims to use its drug discovery capabilities to discover a drug that restores proper functionality to the channel in patients with cystic fibrosis. Based upon the results of the program, the Company and CFFT have agreed to negotiate towards a follow-on agreement under which the Company will explore a structure-based approach for the discovery and commercialization of a drug that will target CFTR, with the financial support of CFFT and subject to a royalty payable to CFFT.
- The second program, which expired in 2007, was focused on the discovery of a small-molecule agonist to the G-Protein Coupled Receptor known as P2Y(2), which plays a role in cystic fibrosis, using the Company's proprietary structure-based drug design system. The Company retains the right to develop and commercialize any drug candidates discovered through this second program, and is obligated to make aggregate royalty payments of up to \$15.0 million to CFFT for the first drug candidate that reaches particular regulatory and sales milestones.

The agreement expires with respect to the first program on August 2, 2009. The second program expired in 2007. CFFT may terminate the CFTR program without cause upon 120 days notice or if the Company suspends or discontinues its business. Either party may terminate the agreement for an uncured material breach.

#### ***Bayer Schering Pharma AG, Germany***

In June 2000, the Company entered into a strategic collaboration agreement with Bayer Schering Pharma AG, Germany pursuant to which it granted Bayer Schering Pharma AG, Germany an exclusive license to co-develop and market Vasovist worldwide, excluding Japan. In December 2000, the Company amended this strategic collaboration agreement to grant to Bayer Schering Pharma AG, Germany the exclusive rights to develop and market Vasovist in Japan. Generally, each party to the agreement will share equally in Vasovist costs and profits in the United States. Under the agreement, the Company retained responsibility for completing clinical trials and filing for FDA approval in the United States and Bayer Schering Pharma AG, Germany is responsible for clinical and regulatory activities for the product outside the United States. In addition, the Company granted Bayer Schering Pharma AG, Germany an exclusive option to develop and market an unspecified vascular MRI blood pool agent from its product pipeline. In connection with this strategic collaboration and the amendment to its strategic collaboration agreement with Covidien, as further described below, Bayer Schering Pharma AG, Germany paid the Company an up-front fee of \$10.0 million, which the Company then paid to Covidien. Under the agreement, Bayer Schering Pharma AG, Germany also paid the Company \$20.0 million in exchange for shares of the Company's common stock. The Company may receive up to an additional \$23.2 million upon the achievement of certain milestones, including \$1.3 million that may be earned upon U.S. product approval. The Company also is entitled to receive a royalty on products sold outside the United States and, if and when Vasovist is launched in the United States, a percentage of Bayer Schering Pharma AG, Germany's operating profit margin on products sold in the United States.

Under the terms of the strategic collaboration agreement with Bayer Schering Pharma AG, Germany, either party may terminate the agreement upon thirty days notice if there is a material breach of the contract. In addition, Bayer Schering Pharma AG, Germany may terminate the agreement at any time on a region-by-region basis or in its entirety, upon six months written notice to the Company.

## EPIX PHARMACEUTICALS, INC.

### NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

In May 2003, the Company entered into a broad alliance with Bayer Schering Pharma AG, Germany for the discovery, development and commercialization of molecularly-targeted contrast agents for MRI. The alliance was composed of two areas of collaboration, with one agreement generally providing for exclusive development and commercialization collaboration for EP-2104R, the Company's product candidate for the detection of thrombus, and the second agreement covering an exclusive research collaboration to discover novel compounds for diagnosing human disease using MRI. Under the first agreement, Bayer Schering Pharma AG, Germany had an option to the late stage development and worldwide marketing rights for EP-2104R. On July 12, 2006, Bayer Schering Pharma AG, Germany notified the Company that it declined to exercise this option. As a result, the Company retained commercial rights to EP-2104R. In the event EP-2104R is commercialized, the Company is obligated to pay Bayer Schering Pharma AG, Germany a minimal royalty limited to a portion of the funding the Company received for this program from Bayer Schering Pharma AG, Germany. The second agreement related to the broader research collaboration concluded in May 2006.

On May 8, 2000, the Company granted to Bayer Schering Pharma AG, Germany a worldwide, royalty-bearing license to patents covering Bayer Schering Pharma AG, Germany's development project, Primovist, an MRI contrast agent for imaging the liver, which was approved in the European Union in 2004. Under this agreement, Bayer Schering Pharma AG, Germany is required to pay the Company royalties based on sales of products covered by this agreement. This agreement expires upon the last-to-expire patent covered by the agreement unless terminated earlier by either party because of the material breach of the agreement by the other party. Also on May 8, 2000, Bayer Schering Pharma AG, Germany granted the Company a non-exclusive, royalty-bearing license to certain of its Japanese patents. Under this agreement, the Company is required to pay Bayer Schering Pharma AG, Germany royalties based on sales of products covered by this agreement. This agreement expires upon the last-to-expire patent covered by the agreement unless terminated earlier by either party because of the material breach of the agreement by the other party.

#### Technology Agreements

##### *Ramot*

The Company's proprietary drug discovery technology and approach is in part embodied in technology that it licenses from Ramot at Tel Aviv University Ltd., the technology transfer company of Tel Aviv University. Pursuant to this license, the Company has exclusive, worldwide rights to certain technology developed at Tel Aviv University to develop, commercialize and sell products for the treatment of diseases or conditions in humans and animals. The licensed technology, as continually modified, added to and enhanced by the Company, consists in large part of computer-based models of biological receptors and methods of designing drugs to bind to those receptors.

All of the Company's current clinical-stage therapeutic drug candidates, PRX-00023, PRX-03140, PRX-08066 and PRX-07034, were, at least in part, identified, characterized or developed using the licensed technology, and the Company would be required to make payments to Ramot, as described below, as and when rights to any such drug candidates are ever sublicensed or any such drug candidates are commercialized. In addition, the Company has used the licensed technology in all of its preclinical-stage programs and would expect to make payments to Ramot if rights to any drug candidates were ever commercialized from any of these programs. One of our employees, Sharon Shacham, Senior Vice President of Drug Development, was an inventor of the technology that the Company licenses from Ramot. The Company believes that Ramot shares a portion of any royalty income received with the respective inventors and, accordingly, Dr. Shacham receives a portion of the amounts the Company pays Ramot.

The Company paid Ramot an upfront fee of \$40,000 upon the grant of the license. Under the license, the Company has an obligation to make royalty payments to Ramot on the Company's net sales of products that are identified, characterized or developed through the use of the licensed technology that are either 1.5% or 2.5% of such net sales (depending upon the degree to which the product needed to be modified after being

## **EPIX PHARMACEUTICALS, INC.**

### **NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

identified, characterized or developed through the use of the licensed technology) and decrease as the volume of sales increases. The royalty obligation for each product expires on a country-by-country basis twelve years after the first commercial sale. There is also an annual minimum royalty payment obligation of \$10,000 per year.

The Company also is required to share between 5% and 10% of the consideration it receives from parties to whom it grants sublicenses of rights in the Ramot technology or sublicenses of rights in products identified, characterized or developed with the use of such technology and between 2% and 4% of consideration the Company receives from performing services using such technology. In connection with the Company's collaborations with Cystic Fibrosis Foundation Therapeutics, Incorporated, Amgen and GlaxoSmithKline, the Company has paid approximately \$2.6 million in total royalties to Ramot primarily for the total payments received to date for the upfront payments and milestone payments received under these license agreements.

The license may be terminated by either party upon a material breach by the other party unless cured within 30 days, in the case of a payment breach, and 90 days in the case of any other breach. The license may also be terminated by either party in connection with the bankruptcy or insolvency of the other party. The license expires upon the expiration of the Company's obligation to make payments to Ramot. Therefore, since the Company has an ongoing obligation to pay annual minimum royalties to Ramot as described above, the license may not expire and may only terminate upon a breach by, or bankruptcy of, a party.

#### ***Covidien (formerly Tyco International)***

In August 1996, the Company entered into a strategic collaboration agreement with Mallinckrodt Inc. (subsequently acquired by Covidien Ltd.), involving research, development and marketing of MRI vascular contrast agents developed or in-licensed by either party. In June 2000, in connection with the exclusive license that the Company granted to Bayer Schering Pharma AG, Germany under its strategic collaboration agreement, the Company amended its strategic collaboration with Covidien. The amendment enabled the Company to sublicense certain technology from Covidien to Bayer Schering Pharma AG, Germany which allowed the Company to enter into the strategic collaboration agreement for Vasovist with Bayer Schering Pharma AG, Germany. Pursuant to that amendment, the Company also granted to Covidien a non-exclusive, worldwide license to manufacture Vasovist for clinical development and commercial use on behalf of Bayer Schering Pharma AG, Germany in accordance with a manufacturing agreement entered into in June 2000 between Covidien and Bayer Schering Pharma AG, Germany. In connection with this amendment, the Company paid Covidien an up-front fee of \$10.0 million and is obligated to pay up to an additional \$5.0 million in milestone payments, of which \$2.5 million was paid following NDA filing in February 2004 and \$2.5 million will be paid upon U.S. product approval. The Company will also pay Covidien a share of its Vasovist operating profit margins in the United States and a percentage of the royalty that the Company receives from Bayer Schering Pharma AG, Germany on Vasovist gross profits outside the United States.

#### ***Massachusetts General Hospital***

In July 1995, the Company entered into a license agreement with MGH pursuant to which MGH granted the Company an exclusive worldwide license to patents and patent applications which relate to Vasovist. The MGH license imposed certain due diligence obligations with respect to the development of products covered by the license, all of which have been fulfilled to date. The MGH license requires the Company to pay royalties on the net sales of products covered by this license, including Primovist, MultiHance and Vasovist. The Company has paid MGH approximately \$0.6 million in royalty payments, primarily related to the sale of Primovist and MultiHance, through 2007 under this license agreement. The license agreement expires on a country-by-country basis when the patents covered by the license agreement expire. The license agreement does not contain a renewal provision. The Company believes that the expiration of these patents does not compromise its proprietary position with respect to Vasovist because Vasovist is covered by composition of

# EPIX PHARMACEUTICALS, INC.

## NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)

matter patents independent of its license with MGH. These composition of matter patents extend into 2015 in the United States, although the life of these patents may be extended.

### 14. Quarterly Financial Information (unaudited)

The tables below set forth unaudited quarterly financial data for each of the last two years:

	March 31, 2007	June 30, 2007	September 30, 2007	December 31, 2007
Revenues:				
Product development revenue . . . . .	\$ 434,392	\$ 395,087	\$ 4,192,766	\$ 5,216,875
Royalty revenue . . . . .	487,658	315,135	100,470	114,406
License fee revenue . . . . .	<u>1,032,850</u>	<u>1,046,458</u>	<u>1,046,459</u>	<u>577,493</u>
Total revenues . . . . .	1,954,900	1,756,680	5,339,695	5,908,774
Operating expenses:				
Research and development . . . . .	13,491,119	14,789,943	14,930,082	14,315,362
General and administrative . . . . .	8,613,758	4,478,387	3,560,010	3,399,738
Royalties . . . . .	53,668	83,428	203,475	254,698
Restructuring . . . . .	<u>—</u>	<u>350,137</u>	<u>—</u>	<u>—</u>
Total operating expenses . . . . .	22,158,545	19,701,895	18,693,567	17,969,798
Operating loss . . . . .	(20,203,645)	(17,945,215)	(13,353,872)	(12,061,024)
Interest and other income . . . . .	1,962,953	1,174,354	927,549	836,250
Interest expense . . . . .	<u>(1,230,734)</u>	<u>(1,252,945)</u>	<u>(504,397)</u>	<u>(1,079,719)</u>
Loss before provision for income taxes . . . . .	(19,471,426)	(18,023,806)	(12,930,720)	(12,304,493)
Provision for income taxes . . . . .	<u>38,089</u>	<u>20,029</u>	<u>—</u>	<u>—</u>
Net loss . . . . .	<u>\$(19,509,515)</u>	<u>\$(18,043,835)</u>	<u>\$(12,930,720)</u>	<u>\$(12,304,493)</u>
Weighted average shares, basic and diluted . . . . .	<u>32,586,377</u>	<u>32,622,318</u>	<u>32,850,191</u>	<u>37,686,382</u>
Net loss per share, basic and diluted . . . . .	<u>\$ (0.60)</u>	<u>\$ (0.55)</u>	<u>\$ (0.39)</u>	<u>\$ (0.33)</u>

**EPIX PHARMACEUTICALS, INC.**

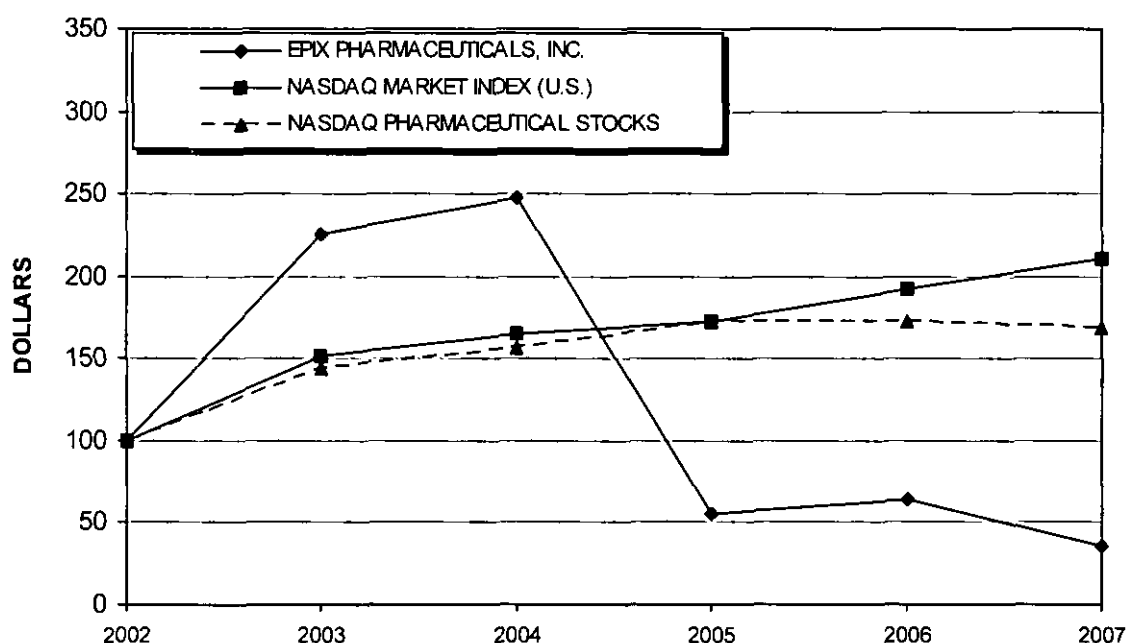
**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS — (Continued)**

	<u>March 31, 2006</u>	<u>June 30, 2006</u>	<u>September 30, 2006</u>	<u>December 31, 2006</u>
Revenues:				
Product development revenue . . . . .	\$ 1,082,867	\$ 731,191	\$ 569,378	\$ 525,966
Royalty revenue . . . . .	457,778	462,718	362,449	320,285
License fee revenue . . . . .	<u>161,597</u>	<u>161,597</u>	<u>413,802</u>	<u>790,914</u>
Total revenues . . . . .	1,702,242	1,355,506	1,345,629	1,637,165
Operating expenses:				
Research and development . . . . .	3,865,001	3,135,417	7,881,361	11,373,221
Acquired in-process research and development . . . . .	—	—	123,500,000	—
General and administrative . . . . .	2,422,528	1,777,927	3,146,316	4,910,549
Royalties . . . . .	43,795	28,233	31,778	959,296
Restructuring . . . . .	<u>289,633</u>	<u>61,472</u>	<u>282,133</u>	<u>—</u>
Total operating expenses . . . . .	6,620,957	5,003,049	134,841,588	17,243,066
Operating loss . . . . .	(4,918,715)	(3,647,543)	(133,495,959)	(15,605,901)
Interest and other income . . . . .	1,304,573	1,410,928	1,519,338	1,261,242
Interest expense . . . . .	<u>(869,363)</u>	<u>(875,631)</u>	<u>(1,082,380)</u>	<u>(2,248,474)</u>
Loss before provision for income taxes . . . . .	(4,483,505)	(3,112,246)	(133,059,001)	(16,593,133)
Provision for income taxes . . . . .	<u>43,816</u>	<u>43,818</u>	<u>31,551</u>	<u>26,128</u>
Net loss . . . . .	<u><u>\$ (4,527,321)</u></u>	<u><u>\$ (3,156,064)</u></u>	<u><u>\$ (133,090,552)</u></u>	<u><u>\$ (16,619,261)</u></u>
Weighted average shares, basic and diluted . . . . .	<u>15,523,207</u>	<u>15,523,207</u>	<u>22,193,441</u>	<u>29,917,696</u>
Net loss per share, basic and diluted . . . . .	<u><u>\$ (0.29)</u></u>	<u><u>\$ (0.20)</u></u>	<u><u>\$ (6.00)</u></u>	<u><u>\$ (0.56)</u></u>

## Performance Graph

The graph below compares the cumulative total stockholder return on the shares of common stock of the Company for the period from December 31, 2002 through December 31, 2007, with the cumulative total return of the NASDAQ Market Index (U.S.) and the NASDAQ Pharmaceutical Index over the same period (assuming the investment of \$100 in the Company's common stock on December 31, 2002 and the reinvestment of all dividends). This graph is not "soliciting material," is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference in any filing of the Company under the Securities Act or the Exchange Act, whether made before or after the date hereof, except to the extent that the Company specifically incorporates this graph or a portion of it by reference.

### COMPARISON OF 5-YEAR CUMULATIVE TOTAL RETURN AMONG EPIX PHARMACEUTICALS, INC., NASDAQ MARKET INDEX AND NASDAQ PHARMACEUTICAL INDEX



ASSUMES \$100 INVESTED ON JAN. 1, 2003  
ASSUMES DIVIDEND REINVESTED  
FISCAL YEAR ENDING DEC. 31, 2007

Our Common Stock is listed on The NASDAQ Global Market under the symbol "EPIX." All prices reflect our 1 for 1.5 share reverse stock split effected on August 16, 2006 in connection with the closing of our merger with Predix

## EXECUTIVE OFFICERS

**Michael G. Kauffman, M.D., Ph.D.**  
*Chief Executive Officer*

**Andrew C. G. Uprichard, M.D.**  
*President and Head of Research and Development*

**Kim C. Drapkin, CPA**  
*Chief Financial Officer*

**Chen Schor, CPA**  
*Chief Business Officer*

## BOARD OF DIRECTORS

**Chairman of the Board: Frederick Frank**  
*Vice Chairman and Director, Lehman Brothers, Inc.*

**Michael Gilman, Ph.D.**  
*President and Chief Executive Officer, Stromedix, Inc.*

**Michael G. Kauffman, M.D., Ph.D.**  
*Chief Executive Officer, EPIX Pharmaceuticals, Inc.*

**Mark Leuchtenberger**  
*President and Chief Executive Officer, Targanta Therapeutics Corporation*

**Robert J. Perez**  
*Executive Vice President and Chief Operating Officer, Cubist Pharmaceuticals, Inc.*

**Gregory D. Phelps**  
*Director, Proteon Therapeutics, Inc.*

**Ian F. Smith, CPA, ACA**  
*Executive Vice President and Chief Financial Officer, Vertex Pharmaceuticals Inc.*

## INDEPENDENT AUDITORS

**Ernst & Young LLP**

## TRANSFER AGENT

**Computershare Trust Company N.A.**

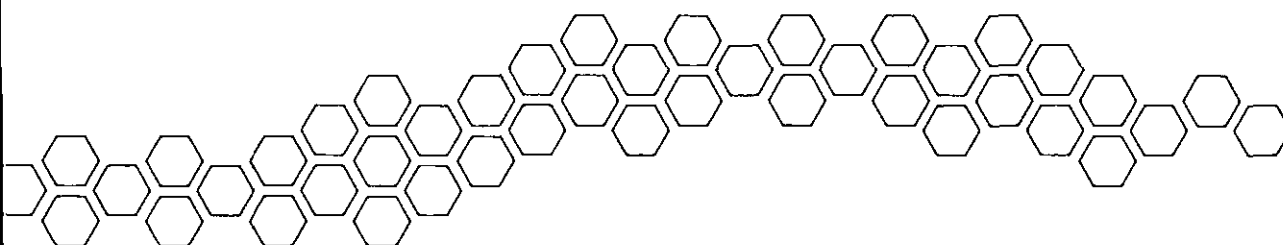
## OUTSIDE COUNSEL

**Goodwin Procter LLP**



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